AIR QUALITY ADVISORY COMMITTEE PUBLIC MEETING

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AUDI-X REPORTING

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THURSDAY, OCTOBER 12, 2000 12:45 P.M.

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DR. OSTRO: We're coming to this AQAC meeting for the year 2000. A couple of administrative things to start. First, thanks to Rachel Broadwin here from our staff of OEHHA for helping to arrange this whole event. And I particularly want to thank all the scientific reviewers who have come to attend this meeting. I know all of you are very busy with your own work and I was just thinking that we have people from every corner of the Continental U.S. We have New York, Atlanta, Seattle, and L.A. covered, so we just need somebody from Kansas City, I think, to make it complete. But we really do appreciate your coming and helping us go through some of the scientific literature here.

Some administrative things: first, bathrooms are on the third floor. There are steps here that you can take down to the third floor and then out to the right. There are restaurants back at the other place for our break if we have time -- actually, we're going to have coffee delivered at the break, so that should be taken care of. We have a Court Reporter here, so everything that is said will be

recorded and on the record. And with that in mind, I just want to make it clear that what we're looking for is comments on the scientific literature. We're not looking for specific recommendations on a level for a standard -- I'll go through in a little bit more detail in my introduction exactly what the scientific issues are. We're not going to be taking any formal "yes/no" votes on things. And as Dr. Kleinman leads the scientific discussion, I think he'll lay out more of the types of issues that we want to try to address. But this is an advisory meeting and review.

Okay, we're now on the record. So this meeting was actually initiated by Senate Bill 25, SB25, so called "Children's Environmental Health Bill." It was enacted last year -- passed last year -- and it specified new requirements for protecting children's health. And there's three general requirements of the bill. One is a Air Quality Standards Review, which I'll be talking about more in a second; second was a review of the toxic air pollutants; and third was the establishment of an air monitoring network throughout the State.

Regarding the Air Standards Review, basically our office, the Office of Environmental Health Hazard

Assessment, with the Air Resources Board, is responsible now for reviewing all the State health-based ambient air quality standards, and with the idea of determining whether or not the current standards adequately protect public health particularly in response to children and infants with an adequate margin of safety. And also within that framework, we're supposed to be determining which pollutant to review first if any pollutants are determined not to be health-protective.

So the Agenda is laid out here and I'm also passing along the copies of all the talks and agenda written out on the first page. And we do plan to stick pretty much to the time framework. It's pretty tight, so bear that in mind. We have to leave this hall at 5:00 today, and tomorrow we'll be starting at 9:00 and hopefully wrapping up around 3:30.

So this scientific review process started with Investigator Reports. The Investigator Reports and the investigators, I'll specify in a subsequent slide. But each pollutant was assigned one experts, or two experts in some cases, and these reports were then sent to OEHHA and the ARB staff. And the idea was to get a summary of the literature -- of the most relevant literature, not an exhaustive

summary -- but to try to look at the scientific evidence that was most relevant for standards review and also most relevant regarding health effects for children and infants. And OEHHA, with support from ARB, the Air Resources Board, then attempted to summarize some of these reports and also incorporate some other information from other sources. And our summaries are included in that report. And the full Consultant Reports, as most of you know, are in the back now in the Appendix of this blue report. We've gone through two public workshops, and this is the third workshop, getting AQAC review, and then we'll be making formal recommendations to the Air Resources Board.

Here's the Investigators listed. And as long as I've got the Investigators listed, let me take this opportunity to say that I reserved a room at a restaurant tonight so that all of the scientific reviewers and consultants could meet and discuss the issues, or discuss the dinner, or discuss whatever they might want to discuss. And it's going to be at an Italian restaurant in Berkeley that's highly recommended. And I think Mike Kleinman will be circulating a sign-up sheet to see if everyone wants to attend. So it's about ten or 15 minutes away from here. There's other places as well, but this is a good place.

So here's the Investigators. And we also have four ongoing AQAC members, Drs. Kleinman, Gong, Balmes and Sherwin. And John Balmes will be here, I think, in a little while, and we're happy to have you back for another AQAC meeting. And we have three consultants that have been invited, Mary White from ATSDR, Kent Pinkerton from Davis, and Dennis Shusterman from U.C.S.F. We also have three members from the Air Resources Board, Shankar Prasad, Deborah Drechsler, and Barbara Weller. We have Bart Cruz here from the Research Division at ARB, Steve Brown as well, and from OEHHA, we have George Alexeeff who is Deputy Director for Science Policy -- Science Affairs, Scientific Affairs, something like that -- and Melanie Marty who is Chief of the Air Toxicology and Epidemiology Section.

So the schedule is that, based on what we hear today and getting public comments as well, we'll be completing a report by November 7th and issuing it to the Air Resources Board. There will be another public comment period and then the Air Resources Board will be meeting in December to review our recommendations. So by the end of this year, we're supposed to review the adequacy of the standards and we're supposed to then take two years to review that standard which is given the highest priority for

review. And then after that two-year period, we'll basically have one year per pollutant for any other pollutants that we need to review and potentially revise.

We have eight different State standards that we're going to be looking at today, and we're actually going to be combining PM-10 and sulfates, so it's actually seven different sessions leading off with Hydrogen Sulfide. And in our own review in determining the prioritization, as well as which standards we thought might not be currently protective, we used five different criteria. We looked at first the extent of the evidence of health effects reported at or near the current standard. Secondly, we weighed the nature and severity of those health effects, whether we were talking about hospitalization and mortality vs. maybe some very mild and reversible effects. We looked at the magnitude of the risk expected. We looked at the evidence indicating that children may be a particularly susceptible population. And also we looked at the degree of exposure -- the degree of current exposure -- relative to the standard. So these were the five factors that we used to try to determine the importance of the different pollutants in terms of reviewing them. And basically our results suggest that health effects may be occurring in infants and

children, and other potentially sensitive subgroups, at or near levels corresponding to the current California Ambient Air Quality Standards. And what we did is then divide the standards into two different tiers. For Tier 1, it includes those pollutants for which we thought the scientific evidence indicated that there were potential risks at or near the standard where the evidence was pretty strong. And that includes PM-10 and sulfates, ozone and nitrogen dioxide. This is the OEHHA and ARB recommendations. And Tier 2 included those pollutants for which the scientific evidence was less certain about potential risks or the effects were maybe occurring at levels higher than the current standards, or where public health protection might be provided through other regulatory programs throughout the state. And that included lead, hydrogen sulfide, carbon monoxide and sulfur dioxide.

So the specific questions that we want to address today is whether you basically agree with our recommendations regarding these two tiers about the adequacy of the current standards in protecting susceptible populations, particularly children and infants; and second, if you do agree with our tiers, which pollutant should be the first one that we begin to review and possibly revise.

So I will now turn the meeting over to Michael Lipsett, who will provide a summary for the first pollutant, hydrogen sulfide. I guess one other comment just about how we intend to work each of the pollutant reviews, either Michael or I will provide a very brief summary of our summary of what our recommendation was, and then we'll turn it over to Michael Kleinman to begin the scientific review, and then Michael will then summarize, I think, what his sense of the scientific discussion is about five minutes before the end of that period. Okay? So Michael Lipsett.

DR. LIPSETT: Okay, thanks, Bart. As Bart said, either he or I will be giving a very brief -- and this is like a two or three minute summary of our summary. And each of the Investigators will be available to the committee members and other consultants to ask about more in-depth sorts of issues related to the science. Okay, so I want to start with hydrogen sulfide. The principal sources for this in California are sewer, gas and petroleum refining and geothermal sources. The current standard was set back in 1969 at 30 ppb (parts per billion). And this was sent to protect against odor annoyance, which is the principal health effect expected at this level. Even though biochemically hydrogen sulfide acts a lot like cyanide and

can be lethal at high concentrations, at the ambient concentrations that we're talking about, these are the principal effects -- odor annoyance and the associated symptoms of headache and nausea.

Now this 1969 study was based on a rounding-up of the geometric mean odor detection threshold based on a study done by the former State Department of Public Health. And then in 1985, John Amoore did a literature review and analysis of a variety of different odorants for the Air Resources Board, and summarized 26 studies that had looked at the odor detection threshold for hydrogen sulfide. And what he found was that the geometric mean of those studies was actually 8 ppb, which is about a quarter of the standard. And interestingly, of those 26 studies that he had evaluated, they did not include the one that had been done by the State Department of Public Health. Now he had also estimated in this report that exposures at the current level, or the current standard, were likely to be annoying to about forty percent of adults. And he indicated also that olfactory sensitivity tends to decline with age so that, say, a 16-year-old might be expected to have an odor detection threshold of about 4 ppb, whereas someone who is around 60 or so, it would be four times that. So basically,

we put this at a relatively low priority. We put it in Tier 2 in part because the levels found throughout most of the state are very very low relative to the standard and in part because the effects that one would expect from exposure to hydrogen sulfide at the ambient level are really not very serious compared with those of the other pollutants. So that's basically it. Michael, do you want to take over now?

DR. KLEINMAN: Thank you. What I'd like to do is first ask Jim Collins if he has any amplification that he'd like to make to what Mike Lipsett has just given us.

DR. OSTRO: The Reporter just asked me to have each of us identify themselves before we speak.

DR. COLLINS: Okay, that was Bart Ostro. Jim Collins. One of the reasons it was assigned to local staff to review this is because we had recently developed acute exposure levels and chronic exposure levels for hydrogen sulfide for the Air Toxics Hot Spots Program. And our acute levels are one-hour exposure. And basically for that, we selected the Ambient Air Quality Standard. For the chronic, we used a study in animals and used various uncertainty factors and other adjustments. And that's why basically we took our reports, combined them, and in addition to some of the earlier knowledge about hydrogen sulfide from the State

Standard to come up with our report because basically we had looked at these chemicals recently. And I don't have much more to add to that except one of the things that has changed is the American Thoracic Society said that something that interferes with your quality of life can be considered an adverse health effect. And I don't know how low kids can detect the stuff. And after a while, sometimes after you detect something that stinks, just when you smell it again, it brings up various psychosomatic things. But again, the State standard is not that often exceeded. And I can certain agree that right now, based on the data available, Tier 2 is an appropriate place to put this chemical.

DR. KLEINMAN: Okay, I'd like to open this up to any comments from members of the committee or the consultants.

DR. GONG: This is Dr. Gong. I have two comments. One is a question. Do you have a feel for the number of complaints of odor problems related to hydrogen sulfide in the State?

DR. COLLINS: Not recently, but we could check with the Air Districts.

DR. GONG: I mean, I would imagine maybe by land fills or other things, but again, is it really due to

hydrogen sulfide as opposed to other things? And I know the measured concentrations may be low, but there are still complaints of odors.

DR. COLLINS: Sure. And some of the things have been like schools in Contra Costa County near the refineries, but it's probably not just H2S, it's probably total reduced sulfur or --

DR. GONG: So it may be a tough situation to dissect.

DR. COLLINS: Maybe it shouldn't be looked at just in isolation for some of those complaints and I don't know about -- some people from the South Coast Air District are here today, whether they have a feel for recent complaints that might be due to hydrogen sulfide?

DR. GONG: Okay, just something that came to my mind. And the other item was this review by Amoore in 1985, I was struck by the comments here and I was wondering, do we know about the quality of these studies -- the scientific quality of these studies?

DR. COLLINS: Well generally, they appeared in either respectable text books or the peer review literature. They were very heterogeneous, but they weren't just sort of unpublished industry reports, they were something that at

least seemed to have some peer review to them.

DR. LIPSETT: Nevertheless, the odor detection threshold -- oh, I'm sorry, this is Michael Lipsett, yes -- span five orders of magnitude, which is pretty unbelievable. There was probably a substantial heterogeneity in the quality of the studies that were done.

DR. GONG: And I assume that there is no data in children, so we really have --

DR. COLLINS: A little bird just told me something. There's an air district in Lake County. And earlier, around the geysers, the levels were often around 30 ppb. And there were lots of complaints from people. Now it's more like 4 or 5 ppb and it's much less complaints, so that's sort of anecdotal. Robert Reynolds, who is the air pollution control officer up there, has been very concerned with sulfur odors for the last 20 years. And so if people are happier up there, it's probably improved.

DR. GONG: I was just commenting. I assume that there's virtually no data on children's response to hydrogen sulfide?

DR. COLLINS: Not specifically to hydrogen sulfide. There is some data on other odorants, but that might be of interest, something that could be pursued if

people are interested in the problem.

DR. GONG: Certainly for SB25, that would probably be a reasonable research area to look into perhaps.

DR. COLLINS: Sounds interesting, yeah.

DR. BALMES: Deborah?

DR. DRECHSLER: As to where there are actually complaints, they do get complaints on hydrogen sulfides in the Santa Barbara area. The offshore oil platforms produce more gas than oil, and it does have a lot of sulfur in it. And periodically, the platforms vent so that they don't blow up, and it kind of smells up the community, but I don't have any idea what the concentrations would be. It would be substantially diluted by the time it hits shore because the platforms are a minimum of two miles offshore.

DR. SHERWIN: Just a quick comment which pertains to effects of hydrogen sulfide. Other than odor, there are potential pathophysiologic effects that I had not heard much about. For example, a lot of people that are on chemotherapy, a little nausea and vomiting would be greatly potentiated by something that's noxious smelling. Secondly, pregnant women who can get easily nauseous and undergo vomiting. So the big question is, aside from the annoying smell, do we have any data pertaining to adverse

pathophysiologic effects like exacerbation of nausea and vomiting in people who are susceptible, like chemotherapeutic people and pregnant women, in particular.

DR. LIPSETT: I'm not aware of any data like that, Jim. Do you know of something? This is Michael Lipsett.

DR. KLEINMAN: Uh, Jim, this is Mike Kleinman. I was just wondering, in looking at some of the health indicators, the one article by Kilbourne and Washburn on finding neurophysiological effects, would you be able to comment on that study, whether --

DR. COLLINS: Well, first of all, I feel it was somewhat anecdotal and I believe Kilbourne is on the faculty at Southern Cal. Maybe Dr. Gong would be more familiar with -- and there weren't that many actual measurements, but it was sort of like it's in the literature, it's just something to go on. And certainly I'd like to see a more complete study, but at least it seemed to be relevant to the topic.

DR. KLEINMAN: But it was interesting that he was reporting effects down at about 10 ppb in that study, which --

DR. COLLINS: Well based on the Amoore study, there would be a lot of people who could detect at that level, and some people could be annoyed based on the

distribution that's expected.

DR. WHITE: I had a question. This is Mary White. Do we have a sense of how many people in California may be exposed to levels that are considered at least annoying? Is it just a few neighborhoods near a few facilities, or do you have a sense of the magnitude here?

DR. COLLINS: I would not say it's wide-spread, but there are "hot spots." There are the geysers, there are the oil companies, paper mills. Sometimes where supposedly there were five million pounds of hydrogen sulfide emitted from hot spots facilities a couple of years ago. Obviously, they're hopefully not all in one area, but there's a little bit, I think, predicted from each oil drilling operation. I think it's more scattered in specific areas, rather than widespread. That would be my impression.

DR. WHITE: But the number of children who may be exposed -- are we dealing with like in the 100's, the thousands?

DR. COLLINS: I think it would be thousands we're talking about right around oil refineries. There's one school not far from where I live and they're talking about relocating it because it's so close to a refinery where there's often malodorous sulfur compounds coming out.

MS. MARTY: This is Melanie Marty. Just a comment on that question. The oil refineries in California are located in populated areas. It's either the San Francisco Bay Area or along the Southern Coast, so H2S does impact a lot of people.

DR. KLEINMAN: In terms of the levels SO2 in the environment --

DR. COLLINS: S02?

DR. KLEINMAN: I'm sorry, H2S, hydrogen sulfide, in the area, I looked at the graph that was in the report which shows that it's been going down and that the peak concentration -- the peak one-hour concentration -- was on the order of about 20 ppb if you eliminate the town of Trona which has very high concentrations. And it would be interesting in a graph like that if we could get means and standard deviations so you could get an idea of how often standards are exceeded or the critical level would be exceeded. But do you have any feel for --

DR. COLLINS: I think the ARB would. It collects that data and would have more idea than we would about it.

DR. KLEINMAN: But that might give some insights into how many people and how widespread the problem is.

DR. COLLINS: We may learn a lot just by

reanalyzing data we already have rather than finding new data.

DR. KLEINMAN: Are there any other comments from the reviewers or participants? Good, we're ahead of schedule. So I think that the sense of the discussion was that some other
pathophysiology might be considered, including the effects on people with chemotherapy or pregnant women who might be more susceptible to the effects of odor to see if there's anything in the literature about that. And probably an assessment of the level of complaint - the number of people that might be exposed -- would be very useful to help really solidify whether you want to perhaps upgrade the problem. If it really impacts on a large number of people, it may make it more of an important problem to study than otherwise. Yes, Bart?

DR. OSTRO: Yeah, a question for ARB, for Melanie, regarding the refineries and what about the replacement of the monitors relative to the refineries? Are the current monitors picking up relevant population exposure from those sources pretty well? Or do you know? Bart [Cruz], do you know? Or ARB?

DR. CRUZ: This is Bart Cruz. I don't think

there's very much H2S monitoring going on in California right now. I know there's monitors in the geysers area and Trona. But I think the monitoring in the rest of the State is being phased out because levels are so far below the standard, but that's certainly information that we can include in the revised report, plus we can get the standard deviations that you'd requested as well.

DR. WHITE: Just as a footnote, H2S has been an issue that ATSDR has had to deal with and it is a problem in a number of communities, particularly when the scientific literature on potential health effects is basically non-existent. So we have a couple investigations ongoing now, looking at potential adverse effects, both neurologic and hospital admissions for asthma. But we don't have results, so this is maybe in the future we'd have something to report.

DR. COLLINS: What areas of the country?

DR. WHITE: This is an investigation that was being done in Dakota City, Nebraska. There are a lot of sources of H2S there, including a very large tannery.

DR. KLEINMAN: Were there any more comments on H2S? Shankar?

DR. PRASAD: Shankar Prasad. Under a separate

program under the same SB25, there is supposed to be monitoring that is about to begin in the later part of the year. And in that selection, Bart, where we are going to determine the adequacy of the monitoring that will represent the children's exposure and the population exposure, then would you effect community out of school or whatever the data is chosen that the committee's recommendation to suggest that H2S be included for monitoring in that particular side? Because SB25 also requires -- I mean, it has many different aspects of it so there will be some monitoring across the state that, to begin with, it will be six to eight sites. And some of the sites under consideration are around the refinery impacted areas kind of a thing, not necessarily as the fence line, but more in the vicinity of the refineries.

DR. GONG: Dr. Gong. I think that's a reasonable way to do it. And again, it's probably going to be the odors that the community is going to sense first and have complaints about. And this would fit very nicely into that. And also, as an aside, do you remember, Shankar, if Bates 2 actually looked at hydrogen sulfide?

DR. PRASAD: No, Bates 2 did not include H2S.

DR. GONG: Okay, thanks.

DR. KLEINMAN: Well, if we've exhausted the comments on H2S, we can move on to the next pollutant, which I believe is SO2.

DR. OSTRO: There's been a suggestion that if we have time left in our block for a pollutant, that we can open it up. At that time, the public comment rather than having public comment rather than having public comment only at the end. So if that's okay with you, I would open it up. We have another five minutes. If anyone else wants to make any comments on H2S.

MS. MARTY: I just have one comment. This is Melanie Marty. I just had one comment in regard to the question about concentrations being monitored in communities. I don't think anyone from the Bay Area Air Quality Management District is here, but at one time several years ago, they were requiring the refineries to put total reduced sulfur monitors at the fence line. So there may actually be a chunk of data that we can get from them to take a look. I don't think they separated out H2S from all the other reduced sulfur compounds, so it's a little dicey to look at that data. But it would be worth getting.

DR. KLEINMAN: Any other comments? Yes, Deborah?

DR. DRECHSLER: We may also be able to get some

actual monitoring data from Santa Barbara County because early this year there were some major emissions from one of the oil platforms and the neighborhood raised such a complaint about it that the owner of the platform is being required to provide several monitors in the neighborhood most impacted by the facility.

DR. KLEINMAN: Well, if there are no further comments, we'll move on to sulfur dioxide.

DR. LIPSETT: Okay, thank you. Okay, for sulfur dioxide, there are two standards in California, a one-hour standard at .25 ppm and a 24-hour average standard set at .04 ppm. The one-hour standard was based and intended to protect exercising asthmatics. It's based on a number of controlled exposure studies that have been done. And in general, asthmatics tend to be substantially more sensitive to the effects of SO2 than people who are not asthmatic. And actually, Dr. Koenig as well as Dr. Dean Shepard in U.C.S.F. were the individuals that discovered this in 1980 and '81. The 24-hour standard is based on epidemiologic studies principally in the U.S. and Europe, and is intended to protect not only asthmatics, but others with chronic heart and lung disease, as well as children and the elderly. In reviewing the controlled exposure studies, there are

consistent effects on asthmatic symptoms and lung function when the exposure concentrations are at .4 ppm and above, although there have been several reports showing effects at least on lung function at down to .10 ppm. And I think it's three out of the four studies that have demonstrated effects at .10 to .25 ppm have used mouthpiece exposures as opposed to sort of normal oral/nasal type of breathing. Now if SO2 is inhaled using a mouthpiece, basically this bypasses the normal defenses of the nose. It tends to be extremely efficiently scrubbed out in the nose, so that if one is breathing with their mouth closed, for example, that very very little of the SO2 will get down to the sensitive irritant receptors at the larynx and below. Now the other one study done at .25 ppm that did not use a mouthpiece, the Investigators tried to replicate that using a somewhat higher workload, and were unable to do so. So in general, our assessment of the literature is such that we feel that there's pretty much of a reasonable margin of safety built in to protect these exercising asthmatics by having it set at .25 ppm. However, this is one thing we would like to get feedback on from the committee and from consultants here is what kind of weight we should accord these studies that show effects at least on lung function down at .10 ppm using

mouthpiece types of exposures. And also, with respect to the exposures to SO2 throughout the State, as with hydrogen sulfide, these are generally relatively low compared to what the State standard and one-hour standard is. For the 24-hour standard, there have been a variety of different outcomes observed in epidemiological studies, including increases in daily mortality, hospitalization, asthma exacerbations, decreased children's lung function, and a variety of other indicators of respiratory morbidity. There have also been a couple of studies done in the U.S. and China suggesting effects on birth weight as well as on, I think, premature delivery. Several of the recent studies, particularly in Europe, suggest these associations with pretty low ambient sulfur dioxide concentrations. They're either at or below the level of the 24-hour standard that we have in California. However, in most of these studies, at least the ones that I have looked at, there's either substantial co-variation between the sulfur dioxide and particles, or these are done using single pollutant models, not adjusting for the other pollutants. And when other pollutants are included in these models, in general, the effect of SO2 goes away. This is not true of a number of the studies done in Europe though recently in which SO2

appears to have the strongest effect of a number of the pollutants that have been looked at. So input that we would like from the committee on this particular standard also has to do with what kind of weight we should accord to these kinds of studies that appear -- there are several that do appear to show an independent effect of SO2, however, one can't be sure if this is really SO2 itself or SO2 acting as an indicator for traffic or other kinds of pollutants as well. So basically, we've put this in Tier 2 in part because we felt that the standards that we have are reasonably protective. Certainly the one-hour standard we think is reasonably protective. But again, the governing factor really is that exposures throughout California to SO2 are in general much much lower than the ambient standards at this point. So, Mike, do you want to take it from here?

DR. KLEINMAN: Thank you. I'd like to ask Dr. Koenig to comment and review.

DR. KOENIG: This is Jane Koenig. I have a couple of things that I want to say about SO2. One is in response to Michael Lipsett's comment that a number of the controls that have been carried out with the mouthpiece, which is an artificial route of exposure to some extent, I think we need to remember that we're trying to protect children with

asthma who may also have allergy. And some of the children in that population are obligatory mouth breathers because of chronic nasal congestion. And so that's just one factor to keep in mind. It's certain true that the nose does scrub SO2 to some extent, but we did one study looking specifically then at the nasal effects of sulfur dioxide and scrubbing the SO2 out is not without some physiological consequences. And the consequence of course is increased nasal worse [phonetic] breathing, which would be probably expressed clinically as nasal congestion. And so that's something else to think about. When we went over this review of the literature, my comments in general about sulfur dioxide is that since we can never be certain at what concentration each sensitive child will respond, we really must limit the emissions as much as possible. And I don't know how close you are to that in California, in that children will always be at more risk because they spend more time outdoors, their lungs and immune system are immature. They have higher lability rates regardless, especially younger children. And SO2, among the EPA criteria pollutants is most in the need of a short term standard, I believe. That has a lot to do with the physical chemical properties of sulfur dioxide. When it is emitted into the

air, it can be transformed fairly rapidly. And also, the emissions -- most of the criteria pollutants, not H2S, I guess, and lead, are we're talking about mainly being emitted from the mobil fleet. And therefore, there's just widespread exposures. SO2 still tends to be more of a point source emission and it's sensitive to upsets in control technology, upsets meteorlogically when there can be down drafts. These down drafts could bring a relatively high concentration of sulfur dioxide into the air for a brief period of time. And I think because of that, I don't as much have a concern about the concentration -- 250 ppb that is chosen for your short-term standard -- but I do have a little -- I mean, if you interpret the scientific control exposure in literature literally, we would assume that that averaging time should not be one hour, it should be ten minutes or 2-1/2 minutes. These may not be feasible, although a 15 minute standard might be feasible. We know that that is all the time it takes in a controlled exposure to elicit dramatic bronchial constriction in subjects who have asthma. That may be all I was going to say at this point.

DR. KLEINMAN: Thank you very much. We'd like to open it up to members and consultants of the committee for

comments.

DR. GONG: This is Dr. Gong. I think Dr. Koenig did an excellent review and I did have a question about the comment regarding inflammation with SO2. One comment is that she noted that the Swedish investigators reported cellular inflammatory effects in healthy people breathing 8 ppm SO2 for 20 minutes as opposed air exposure. And that's obviously an industrial or occupational type exposure. I think some Australian investigators looked at .25 ppm and reported it at the ATS meeting. And they found no inflammatory cellular changes in induced sputum. And I was wondering if you had any comments about that. You seem to consider it in your last sentence to be a very important end point.

DR. KOENIG: Well, I certainly agree with Dr. Gong that 8 ppm is something that we're not concerned with. I think maybe Dr. Sanstrom has repeated that study at 4 ppm, I can't remember. We in our laboratory did expose -- I believe it was young adults with asthma -- to sulfur dioxide via I think a face mask. And we looked for signs of nasal inflammation. And this has been published -- Bechtold [phonetic], or whatever, in the references. We found an increase in neutrophils in the nasal lavage fluid after SO2

exposure that we didn't see after air exposure. So there may be some possibility of getting some inflammation. However, certainly, if you look at the bulk of the literature, it's certainly rapid bronchial constriction that seems to be the clinical end point of our concern. And what does the last sentence say?

DR. GONG: Well, your own words, "It is generally agreed upon that airway inflammation is a more adverse effect than reversible PFT's."

DR. KOENIG: Well, yeah, that's a generic statement that inflammation is considered to be more -- if we look at the American Thoracic Society guidelines on adverse effects, inflammation would be considered more important. I should perhaps divorce that a little bit more from the above statement. I think even though it's certainly true that there are no studies showing airway inflammation, perhaps at low concentrations in asthmatics using bronchi alveolar lavage techniques, as far as I know, there are no studies conducted doing that either. And so we really can't say one way or another whether those effects would occur.

DR. GONG: Just parenthetically, we recently completed and --

DR. KOENIG: No fair!

DR. GONG: Fair is fair -- we've done a study in which we actually show that there is a ucenophillic [phonetic] inflammation in induced sputum of asthmatics exposed to 0.75 ppm of sulfur dioxide for ten minutes.

DR. KOENIG: Okay, so a profit.

DR. GONG: Yes.

DR. KLEINMAN: Dr. Gong, how long were the exposures?

DR. GONG: Ten minutes.

DR. THURSTON: George Thurston. You know, just seeing that up there unaccompanied by PM or MO2 makes me think of the fact that SO2 exposures would never be in the absence of PM. And I know, if you recall the experiments of Mary Amdur and L.C. Chen have done, the effects of SO2 are greatly enhanced when in the presence of particles. And this whole question of mouth breathing vs. nose breathing is important, except if you consider the sort of escalator effect of particles allowing the SO2 to permeate deeper into the lung, albeit now as a particle, not a gas. But I'm wondering if there are experiments addressing that issue where people have been exposed to SO2 in the presence of -- let's say you take an ambient aerosol and then you add SO2

and see if there's more of an effect than without the SO2, that kind of thing.

DR. KOENIG: Oh, well, those studies certainly have been done. For those of us who have been in the field for a long long time, we remember Robert Frank at the University of Washington started a very ambitious study of sulfur dioxide droplets. And in this case, the carrier particle was sodium chloride, a particle that in and of itself would not be expected to cause physiological problems and changes. And there were a number of studies done initially in guinea pigs and those were associated with changes in airway resistance and in dynamic compliance which is the kind of stage you can do in animals. And then we came along and started doing these studies in healthy adult volunteers and then ultimately then in children with asthma. And in the study that Michael Lipsett referred to that we published initially in 1980, those studies were done with SO2 plus sodium chloride droplets. And, of course, we were testing the hypothesis that you have mentioned, that the droplets would carry the SO2 down deeper into the lung. And I don't know whether we were ever able to sort that out completely. We did studies later looking at SO2 alone compared to SO2 plus the droplets. And the pulmonary

function changes seemed to be about the same. But in terms of what you also brought up in your statement, again, talk about mouth exposure vs. nasal exposure. There have been studies of SO2 exposure by nose, nasal exposures that have been associated with increased bronchial constriction. So apparently, some of the SO2 is getting down there past the nose. And I think that the initial studies that were done by Bob Frank, again, and Frank Spizer [phonetic] when they looked at nasal uptake of SO2, those studies were done during quiet breathing. And the uptake perimeters are very dependent on mellituria [phonetic] rate, as I'm sure Michael Kleinman can tell us.

DR. FRAMPTON: Mark Frampton. I'd just call attention to a paper I reviewed for the NO2 review which Devalia and his group in the United Kingdom that exposed people -- mild asthmatics -- to a combination of NO2 and SO2 and found an increase in allergen responsiveness at both 24 hours and at 48 hours after exposure, but only in the two gasses in combination, not to SO2 alone or to NO2 alone. And the concentration of S02 was 200 ppb, so .2 ppm. And these were six-hour exposures. So that has not been replicated that I know of, it's just the one study. And I'm not aware of any other studies looking at SO2. Jane, SO2

effects on allergen responsiveness in asthmatics -- kind of a whole area that hasn't been explored.

DR. KOENIG: No, I'm not aware of any either. I'd forgotten about that Devalia study. That's an interesting comment.

DR. SHERWIN: Sherwin. Are there highly reactive species of sulfuric compounds and are monitoring mechanisms picking them up? For example, ozone has some highly reactive oxidants that we don't measure. Is that also true in sulfuric compounds?

DR. KOENIG: Well, not with SO2. SO2 is a pure molecular composition.

DR. SHERWIN: I was thinking of sulfuric acid, sulfurate --

DR. KOENIG: But sulfates come later when George Thurston will talk about particulate matter, rather than gasses.

DR. SHERWIN: Well, I was thinking of sulfuric acid. To me, sulfates and sulfuric acid sort of have always gone together.

DR. KOENIG: Right.

DR. SHERWIN: And now I'm wondering --

DR. PINKERTON: That would be a particle.

Sulfuric acid in order to be a particulate exposure -- a vapor exposure.

DR. KOENIG: That's regulated, I guess, in California with the zone standard, but USEPA regulates sulfuric acid by manipulating the PM standards.

DR. KLEINMAN: Russ -- this is Mike Kleinman -- we did some studies where we looked at the conversion of SO2 to other chemical forms in the presence of particles. And it turns out that SO2 very rapidly can be converted into bi-sulfates and sulfates through atmospheric chemical changes on the surface of particles, especially if there are oxidant gasses and inorganic ions like iron and manganese present. So that does happen. The problem is that these are very fast reactions and our monitoring can't really look at these things in real time.

DR. SHERWIN: Some of the highly -- high turnovers -- or highly reactives -- are the ones which are most noxious.

DR. KLEINMAN: Right. So what we are seeing are the end products of all these reactions which turn out to be sulfates.

DR. SHERWIN: And then there are sulfites as well as sulfates, and what about those?

DR. KLEINMAN: Does anybody -- yes?

MS. WHITE: This is Mary White. I had a question about this whole mouth breathing issue. In addition to children who may be obligatory mouth breathers, just average kids running around laughing and that sort of thing will breath through their mouth. Somebody must have estimates of what proportion of children spend what proportion of their time breathing through their mouth. Does anybody have that kind of estimate?

DR. KLEINMAN: That's been an area of research that a number of people have looked at. And most people, for example just at rest, breath partially through their mouth, partially through their nose. Very few people are pure nose breathers or pure mouth breathers. But on the order of give or take, people will breath about 15 percent orally and 85 percent nasally at rest. As you get up to about 20 liters a minute, say doubling your minute ventilation, you'll almost be at 50/50, and then it continues to go up in most people. Some people will move up quicker than others. Children tend to follow about the same pattern. I don't think that their breathing pattern has been studied as well as it could be. Most of the studies have been done with young adults. The other thing that's

interesting is the penetration of very water soluble gasses like sulfur dioxide and formaldehyde. These increase not only by the amount of oral/nasal breathing, but also by the rate of breathing. As you ventilate quicker, the ability of the upper respiratory tract to scrub these things becomes diminished because this is really time dependent. So the molecules spend less time in that area and do penetrate deeper.

DR. SHERWIN: Mike, let me add just to bring in a little bit of lightness to it that, aside from children being very active, they also cry a lot. Some do a lot of crying and I would say very cheekily that maybe spanking is never advisable, but if it is, it certainly shouldn't be done on smoggy days!

DR. PINKERTON: This is Kent Pinkerton. Just a clarification for my own interest. Since SO2 is a gas, but it's so highly reactive with water, as has been mentioned, to form sulfuric acid or the sulfurous acid, and those I assume are now considered to be particulates, why would you not monitor SO2 if this is for the fact that if an eventual final product of this is going to be a particulate, why wouldn't you be regulating this as though it were a PM also?

DR. KLEINMAN: I think there's a separate standard

for SO2 as opposed to, at least at the federal level, they don't regulate sulfates except as part of the particulate mix. There is an SO2 standard federally and in-State. Because SO2 does contribute to the particle problem, in some ways it ought to be considered as part of a particle sulphate SO2 mixture, I guess. But we don't have a good mechanism for it, I don't think.

DR. LIPSETT: One other thing -- this is Michael Lipsett -- is that SO2 does have these powerful broncho constrictive effects on asthmatics, but sulfuric acid does not. So the chemical form of it does seem to make a difference in terms of it's immediate health impacts.

DR. PINKERTON: Kent Pinkerton again. But if SO2 isn't held, I assume it would immediately become hydrated. So I guess I'm a little confused as to how it has its effect by itself.

DR. KOENIG: I think it's assumed to be transformed in the mucus lining to a bi-sulfide. And that's another species that we don't measure at all.

DR. OSTRO: Bart Ostro. I have some questions about the implications of some of the epi studies, a couple different issues. First, as Michael Lipsett indicated, there's certainly a lot of studies both in the U.S., but

particularly in Europe, showing SO2 affects -- clearly not necessarily independent SO2 effects -- but certainly SO2 affects things like mortality and hospitalization. And one theory I had heard a couple of years ago was the fear that SO2 might be a proxy for fine particles among other things. And this is a question, I guess, to George Thurston, whether there's been any follow-up on that and what the U.S.E.P.A. line is on the SO2 effects now in some of these epi studies.

DR. THURSTON: Well, I wouldn't be privy to what the E.P.A. thinking is on it right now. Yeah, I think there are occasions where people have thought that SO2 would be a proxy for formation products of SO2, which include acids, which would then be as particles. But there's such a limited sampling of acid products that this hasn't really been studied. So I think it's a hypothesis at this point that's never really been tested fully. So I really don't have a good answer for you. I did want to say something related that occurred to me. You know, this whole question of SO2 vs. PM, there was a paper by Shimmle & Miroski that was done about 1973. And they took advantage of the fact that in New York, they basically took all the SO2 -- sulfur -- out of the fuels that were being burnt in New York in

just a matter of a few years. And what happened was the levels of SO2 dropped dramatically and the particle levels stayed about the same. And I'm trying to remember -- it's published -- it might be in Environmental Health Perspective, or something like that. And what they found was the SO2 was significant, it stayed significant, and its slope went up when the levels went down, which would indicate that it's a proxy for something else. And that sort of fits in with perhaps being a proxy for particles of a certain type. So that would sort of imply that it's the PM, not the SO2, in that situation. It's kind of an interesting study in that it's something that we always would like to have which is some sort of a massive intrusion experiment where you could suddenly eliminate one thing and see if anything happens. So I think that's an interesting paper to look at when you're trying to sort out this SO2 vs. PM question. Anyway, maybe that will help.

DR. KOENIG: There was a paper that was just published in Environmental Medicine by Joel Schwartz -- you've seen that paper --

DR. THURSTON: I'm not sure I have.

DR. KOENIG: I didn't come here to describe the paper, but what he did was he looked back at I think it was

Philadelphia. And since his original analysis in Philadelphia, either SO2 or particles had completely flipped in terms of season -- I think it's particles now that are maybe up in the summer --

DR. THURSTON: Yeah, particles are now high in the summer and they used to be high in the winter.

DR. KOENIG: And so he was able to juxtapose those two things to look at the question is it SO2 or is it particles. And of course, those of us who know Joel Schwartz aren't too surprised to find out that it was particles. But it's a very interesting paper using a new way of creating epidemiology.

DR. THURSTON: Yeah, well, it's sort of a similar concept, but over a much longer period of time. The New York one was worth looking back, as well as that. That's a good study to also look at. But the New York one was just so quick. In about two or three years. And there wasn't this change in particles. I think there were two things going on in Philadelphia, that those SO2 levels went down and the particle levels went up in the summer. So it's a little more complicated story in Philadelphia, but it comes to somewhat the same conclusion.

DR. KLEINMAN: We may have an opportunity to do

the same experiment here in California. If you look at the sources of SO2, you've got the stationary sources which produce a very large fraction, and then off road mobile sources produce almost at much at this point in time as stationary sources. And with the move to cleaner diesel fuels, the SO2 emissions from that are going to drop dramatically. We may actually see our levels drop and a half if the source apportionment is right. So we may actually have a chance to do that experiment.

DR. THURSTON: Well, and in fact the human dose levels will probably drop more than that because cars are where the people are. The SO2 from cars is right there at breathing level, whereas, you know, if you're talking about emissions from a power plant or something --

DR. KLEINMAN: No, these emissions are not from cars, these are from --

DR. THURSTON: Right, yeah, sorry. Yeah, right, but I'm just saying that it'll have a direct impact in cars in this case and diesels as well which are right at breathing level. Yeah, so that is something because I know sometimes I've gone -- I'm at an NIHS Center and I always -- we go down every year and educate Congress people about what

we're doing in terms of research so that they're knowledgeable about the importance of supporting endeavors like research. And that's one of the questions I always get is, "Show me where they've cleaned up the air and there's been a change." And that's very hard to do because there isn't usually that dramatic a change and there's lots of other things going on -- changes in health care systems, which is something you've really got to watch out for these days -- and things like that. So any time that we have an opportunity to study something like this, we ought to put some efforts into documenting it and studying it.

DR. KLEINMAN: Well, I guess when we talk about lead, we bring up that issue again because that was a pretty dramatic case. Bart?

DR. OSTRO: Another question relating to the epi studies, but directed to the toxicologist and clinical people, which is that clearly some of the outcomes that the epi studies are showing are cardiovascular related, not just asthmatics. And I'm wondering from any of the SO2 literature if there's any underlying biological mechanism that could explain any of that.

DR. GONG: Well, I can foresee one possible mechanism and it's all postulated -- this is Dr. Gong -- and

that might be the airways inflammation caused by SO2 inhalation. And you could sort of tie this together a little bit with the particle story as well that's been hypothesized, causing various mediator release and effecting systemically various processes including coagulation and cardiac electrophysiology, etc., etc. So it's within reach. Again, I'm not familiar with any studies in animals that might add to that.

DR. FRAMPTON: Mark Frampton. I would just add that you actually would expect subtle or even not so subtle effects on heart rate variability from an exposure to SO2 because we know that upper airway effects have clear consequences on heart rate and heart rate variability just because of parasympathetic and sympathetic reflex activity. Whether that's in any way connected with the particle mortality and particle cardiovascular mortality issue is completely speculative at this point, but that is something I think to consider and, for future studies, something to think about. We've actually -- I've not seen very much attempt to really study the possible relationship between upper airway effects and some of these cardiac end points. The assumption is usually that the relationship is due to deep lung penetration of material in particles or carried on

particles, and either establishing an acute phase response or endothelial activation, or some kind of direct cardiac effects of a particle component. And none of that would be relevant to SO2 because it's almost completely consumed in the upper conducting airways. But this idea that laryngeal irritation or a little bit of tracheitis from inhaling SO2, certainly that's going to cause cardiac effects if that's occurring in somebody with terrible heart disease that could conceivably have consequences.

DR. KLEINMAN: Well we have a few more minutes that we can use. Are there comments from the public on SO2?

DR. LIPSETT: Actually, before we get to comments from the public, I just wanted to ask the committee members and consultants again about the mouthpiece exposures, I mean the extent to which we ought to be thinking about effects that might be related to mouthpiece exposures vs. more normal route of exposure as something that is important to consider in trying to evaluate the help protectiveness of our one-hour standard. Does anybody else have any comments other than those that were already made?

DR. KLEINMAN: I guess I would make the one comment that the uptake in the upper respiratory tract, whether you breath by your nose or your mouth, is extremely

rapid. And the SO2 taken in by the mouth is still going to deposit in the oropharyngeal. And less then 8 or 9 percent actually penetrates as far as the larynx. So I think you would probably be able to rationalize that a mouthpiece exposure at rest might be not a lot different than what happens to a child when they're exercising. So that may be a reasonable experiment for comparing with an exercise study. My personal opinion is that probably valid studies ought to be given reasonable weight in judgment. But other people may have other opportunity to talk.

DR. GONG: This is Henry Gong. And maybe Jane can comment on this. Didn't Bethel or someone from San Francisco examine the difference in effect from mouth bringing vs. unencumbered bringing?

DR. KOENIG: Yes, yes.

DR. GONG: Do you remember the results?

DR. KOENIG: I think that that's in our report, but maybe not. As I remember the results, nasal breathing compared to mouth breathing was shown to mitigate but not abolish the effect. And that's in agreement with a study that we did that we published in about 1995 on the effects of sulphur oxides in adolescents with asthma, where we had them breathe through a mouthpiece with nose clips in place

vs. a face mask where they could breathe either by nose or mouth. And we looked at both SO2 and sulfuric acid in that study. And we found the same thing, that the decrement in lung function and even airway resistance was less during the nasal route, but it was still significantly different than air exposure. And I think we have to remember that even though a large amount of the SO2 is scrubbed out in the nose, it apparently doesn't take a lot of SO2 in the bronchial airways to cause this effect that we talk about so much.

DR. GONG: I think if you had your choice though in designing a study, I would prefer at least, in my opinion, to go the unencumbered breathing route so we wouldn't even have to worry about this issue. Put it that way.

DR. KOENIG: Well, Henry, I think that there's data from your lab looking at SO2 exposures. Didn't we do any unencumbered vs. encumbered exposures?

DR. GONG: I didn't.

DR. KOENIG: But you've looked at SO2 exposures with various pharmacological interventions. Were those SO2 exposures by mouthpiece?

DR. GONG: Unencumbered -- in chambers.

DR. KOENIG: Unencumbered. So you have a body of data on unencumbered exposures of SO2, and you see pulmonary responses, I believe?

DR. GONG: Yes. So the point of that discussion is that the studies that showed response with just pure oral breathing should not be discounted since oral/nasal breathing also shows responses and it's not just due to the artifact of breathing through the mouth. I think in order to stay on schedule, we ought to move ahead to the next pollutant, so we will have a period later on for public comment.

MS. BROADWIN: There is ten more minutes.

DR. GONG: There is? Oh, you've got a different schedule. I take it back. Okay.

MR. HEISS: I'm John Heiss with Air Improvement Resource. I'd just like to raise a point of information. E.P.A. decided not to set a short-term SO2 standard several years ago that was challenged and it was remanded back to the agency. So they are going through some sort of analysis on the same issue. I was wondering if you all know the status of that and whether there are any reports, or any proposals, or any analyses of exposure and risk associated with that that's available, or may become available in the

future.

DR. KLEINMAN: Is anybody?

DR. LIPSETT: We're not aware of any of these. I don't know if the ARB staff is, but in any case, before we would undertake a revision of the standard, we would certainly be in contact with E.P.A. to see what's going on in their shop. MR. ALEXEEFF: George Alexeeff with OEHHA. And I have a question for Dr. Koenig or whoever on the previous slide, Michael, if you want to move to that one. It's sort of asking the same question that Michael was asking, but maybe a little more specifically. I wondered if this summarizes the information that whether or not the current standard of .25 has an adequate margin of safety.

DR. KOENIG: As I tried to point out earlier, I'm not as concerned perhaps with the concentration where California has the short-term standard set, 250 ppb. But I'm wondering what the justification for the one-hour averaging time is when the data -- most of the SO2 exposures that have been done in controlled laboratory settings are short term. Henry just mentioned his was 10 minutes. We usually have done 10 to 15 minutes. And there was a big review done in the mid-80's by Horstman and Folinsbee where they looked at some of the SO2 literature in adults with

asthma. And the summary of that review was that 2-1/2 minutes was a sufficient duration for an SO2 exposure in the range of 250 or 500 ppb to produce statistically significant decrements in lung function, or statistically significant increases in airway resistance. And so, again, it's not so much whether .25 is right, but how many -- the air modelers could tell us -- how many peaks well above 2.5 in an hour could be there without violating that one-hour standard.

DR. FRAMPTON: I guess one thing to consider in thinking about this and weighing this is my understanding of SO2 exposure in asthmatics is it caused an acute bronchial constriction. It does not cause a late phase asthmatic response which allergen can do, it doesn't have inflammation inducing properties that we know of at these low concentrations. And it resolves quite quickly. Now it's still a health effect, certainly, to drop your FEV-1 as can happen with SO2, but I think that's part of the reason that it hasn't been considered as adverse a pollutant as ozone, for instance, or other pollutants where you have clear inflammation that can last beyond 24 hours. That does not happen with SO2. It's a reflex response, it happens quickly, and it goes away fairly quickly.

DR. KOENIG: I would just like to comment on that

a little bit. Our group in Seattle, who has worked with adolescents with asthma and children with asthma for some time, feel that any air pollution induced decrement in lung function has the potential of making a quality of life change for that child. If they're outside playing with their peers in soccer and they can't keep up and they can't breathe, they may decide to drop off the team or make a major behavioral change in their life. And because of that, we just have to be very careful defining what is an adverse effect for a child exercising outside and what could be the sequelae of having a couple episodes of shortness of breath during exercise. So I think it carries a little more weight than just dismissing it as a transient response that resolves in 20 minutes, which is probably what it does. But what happens then to -- does this somehow change the behavior of that child in a way that we wouldn't really want to be responsible for?

DR. KLEINMAN: I just wanted to point out, this was a topic when the standard was actually reviewed. I believe it was the last time this committee actually met, which was about five years ago. This was actually raised. And at the time, the rationale for setting the standard was not that the standard said the effects over one hour were

important. It was a monitoring issue that we couldn't deal with the reams of data -- reporting the data every five minutes or 15 minutes. And ARB did an analysis -- a statistical analysis -- of the spectrum of frequencies of what you would expect to see. And the standard was set with this number in mind -- and somebody else may have a clearer memory of this -- but that this was a good representative number taking into account the fact that there would be short term levels that were considerably higher, but that this would allow for a margin of safety. And I think what George Alexeeff just raised is the question is, knowing what we know now, five years later, are we still thinking that we have an adequate margin of safety? Given that, if you look at our data on levels, the standard is set at 250 ppb. Our levels of SO2 have gotten down to just below -- the one-hour peaks are now around 150 ppb, which is I guess the number for the worse case spot in the California area. Does that allow us enough breathing space -- that's a pun. Do you have a comment on that, Jane?

DR. KOENIG: So did I understand you correctly to say that the major peaks in a previous 365-day time period did not exceed 150 ppb?

DR. KLEINMAN: One hour average.

DR. KOENIG: One hour average. I would need to look at the 15 minute averages before I would say that we had provided an adequate margin of safety. But I would also -- I don't know how the Air Resources Board functions -- but I'd go back to my introductory remarks where I would say that if an air agency has an opportunity to take action that will keep SO2 emissions out of the community air, reasonable actions, I would really encourage them to do so because I just don't think that public health officials are ever going to be able to say with 100 percent confidence that a particular standard will protect all the children with asthma that are likely to be exposed.

DR. PINKERTON: Kent Pinkerton. I just was curious about how strong this linkage is between SO2 at ambient levels and adverse pregnancy outcomes that was referenced. Is that something that is an issue here?

DR. KOENIG: I'm not sure that we have enough data to evaluate that. I don't know whether George is going to talk about infant mortality and birth outcomes with respect to PM and sulfates. But I think depending on how you read the current version of the PM criteria document, it does appear that we're really beginning to look at some reproductive effects with particulate matter and whether we

need to look at those with all the other pollutants, it could open a lot more -- we could extent these review periods by two more days if we wanted to.

DR. KLEINMAN: Okay. I'm going to break now and I'd like to just point out that John Balmes has arrived. That fills out our committee a little bit. And we'll move on to the next pollutant which is Nitrogen Dioxide.

DR. LIPSETT: Okay, with everyone's permission, I think I'd like to actually change the agenda here to accommodate Dr. Tager's schedule who has to leave early. He's one of the co-authors of the ozone review. So I think what I'd like to do is go on to ozone and then come back to NO2 at the end of the day if that's okay. Are there any objections to that? All right. Hearing none, proceed.

Okay, the current California ozone standard is set at .09 ppm, it's a one-hour average that's based primarily on number of controlled exposure studies that usually have one to two hours duration that basically appeared to show an apparent threshold at somewhere around between .12 ppm. These were studies that were done in the 1980's. Now there have been several studies done by the U.S.E.P.A. since then of using exposures at 6.6 hours and exposure concentrations as low as .08 ppm. And these have showed during the course

of exposure progressive increases in symptoms and in lung function decrements. And at each one of these exposure concentrations, after bronchi alveolar lavage have found both cellular and biochemical indicators of inflammation and increases in airway hyper-responsiveness. The effects seen at .08 ppm were certainly lower than what one sees at .12 ppm, but nevertheless were clearly significant both clinically and statistically. Now there have been a number of epidemiologic studies that have been associated with a variety of acute respiratory effects when the epi concentrations were lower than 0.09 ppm. And these are ones where the most consistent effects observed have been on lung function, even at exposure or at concentrations that are down around .04 ppm. These are not necessarily accompanied by any symptoms, so that the biological significance of these transient effects on lung function is not entirely clear. There are a couple of studies, one done by Drs. Tager and Balmes, and another done at Yale on college freshmen that seemed to show cumulative effects of ozone exposure over the lives of these individuals on lung function, particularly looking at flows of low lung volumes. Now the effects of the transient exposures, or the relationship between the transient and the long term

exposures are not clear. And so it's difficult to draw any type of causal type of relationship at this point with just these two studies. But nevertheless, there may be some concern about significant long term effects on lung growth from repeated exposures to low levels of ozone. Now one of the reasons we allocated ozone to Tier 1 in part was because of the seriousness of some of the effects that have been seen. But in addition, most Californian's live in areas where ozone exposures regularly exceed the current standard, and sometimes by up to as much as a factor of 2. So with that, I'd like to turn this over to Dr. Kleinman again.

DR. KLEINMAN: We have this eminent [inaudible] who actually produced this report, so I'd like to give Dr. Tager a chance and then Dr. Balmes a chance to respond to the review.

DR. TAGER: Ira Tager. I just want to make a few brief comments and then just take the liberty of showing two graphs because, as I indicated in the conclusion to the epidemiology, I agree with Michael's summary. From my point of view, I think the data are pretty convincing from epidemiological studies. But a variety of health effects are occurring at or below the California standard. Whether children are really at more risk than adults is very

difficult to determine from the epidemiological studies. In fact, the one study that I could really find that spoke directly to that, which was looking at asthma hospitalizations, didn't really support that concept. But that's only one study. So I think you have to distinguish the fact that the effects are occurring and whether or not children per se by virtue of age or given age underlying disease would be more sensitive than adults is an open question. But what struck me when I reviewed all of this -- and I'd just like to show two transparencies -- was the first transparency is from a paper looking at effects of ozone on forced biocapacity. And this was a study that Joel Schwartz did using Anne Hanes' data, which is a cross sectional study -- basically population average FEC's and population average exposures -- and it suggested there might be this, if you will, threshold of about 40 ppb. And I provided several examples of other studies that have shown that. But I'd just like to show one other one because -- and this is from a study that was done in Mexico City. And the reason I wanted to show these is it's strikingly similar, and it shows a couple of things. First of all, the dots here -- there are several different models that would come from the Mexico City study. And these were kids on a

treadmill essentially exercising in ambient ozone concentration. And the dotted line here is from Bill McDonnell's analysis -- the aggregate analysis of the exposure chamber data. And there's a striking similarity between the population cross sectional data, exposure data across a wide range of ozone, and then sort of real world individual data in ambient concentration. So I think one of the things that comes out of this, is this may be a situation and we may have some idea of the boundary, if you will, of where health effects may be occurring. Now I don't know that we know it exactly, but it makes, from my point of view, a pretty convincing argument here that there may actually be at least over both the short and long term. If you take the cross sectional studies to really reflect long term exposures, there may be some threshold effect and that that will have to be considered in so far as ozone is actually exerting an effect in and of itself, rather than being a marker for some other more complicated pollutant regimen. I think that's all the comments I specifically wanted to make.

DR. KLEINMAN: Thank you. Dr. Balmes?

DR. BALMES: So John Balmes. And if I could step up to the overhead. Just a couple points. This is in our

section, but just to remind everybody, in '87 when ARB reviewed the ozone standard, there was this statement, "Pulmonary function decrements occur in healthy exercising adults and children exposed to concentrations as low as 0.12 ppm for one to two hours. Such changes were not demonstrated at levels between 0.10 ppm and 0.12 ppm," and that that was the case in 1987, but it's clearly not the case anymore in terms of the data. And I'm going to show you a figure from a federal E.P.A. criteria document that's in our section, which summarizes the pulmonary function data from the 6.6 hour protocol studies at Chapel Hill at 0.8, 0.10 and 0.12 ppm. And you can see that there were mean decrements that are fairly impressive by the 6.6 hour end of exposure time point. But something I didn't include in our section that many of you may be aware of from reading the federal E.P.A. report, when you look at the percentage of individuals who had greater than 10 percent decrements in FEV-1 in these studies, they're in fact -- was the dose relationship 26 percent of the people exposed to 0.08 ppm for 6.6 hours with intermittent exercise, going up to 46 percent at 0.12 ppm. These are young male adults. But there's no reason to suspect from the literature that kids would be any less sensitive. And then, just to make the

point again, the same 6.6 hours protocols that E.P.A. used for the pulmonary function testing -- and I should say airway responsiveness also increased in a dose related way with the three increasing concentrations in those studies -- but they also did studies of airway inflammation involving bronchi alveolar lavage end points. And in fact there were significant changes in a number of inflammatory or lung injury markers. I think it's also fairly clear from multiple studies that persons with asthma have enhanced airway inflammatory responses to ozone and that has to be taken into consideration with regard to any revision of ozone air quality standards. And asthmatic responses to allergen are enhanced by ozone. And the study that started this work in humans at any rate, the Mulfino study, while small in total number of subjects, potentially flawed in study design, did in fact show an effect -- an ozone effect -- to enhance allergen allergic responses at one-hour resting exposure to 0.12 ppm. And I just want to take a second to make some corrections in the section. Page 6 in the second paragraph, the second sentence describes a Krishna, et al. study, it's reference 19, that sentence should indicate that the exposure was for two hours -- 0.12 ppm ozone for two hours. That's perhaps the -- yeah, that's

the shortest exposure to 0.12 ppm ozone that's showed an inflammatory effect. And then the Kinney study, by reference 26 on page 7, so that's the second full paragraph, there are a number of typos with regard to the concentrations of ozone. The maximum ozone concentration in the summer of '92 was 0.11 ppm. The mean should be 0.058 ppm. In the following winter, 0.064 mean = 0.032. And then the maximum concentration in Summer of '93 was 0.14. Mean should be 0.069. But the Kinney study did show some evidence of an ozone effect in adult joggers on Governor's Island in New York at levels below 0.12 ppm. And then two studies of children by Frisher, et al. in Germany again using nasal lavage end point suggested ozone induced inflammation at levels at 0.09 and above. Actually, that was the high level of ozone in those studies. The low level was below 0.07 ppm. And there was actually a difference between the two. There could have been a dose response at the lower level, but they actually didn't analyze the data that way. So I think in summary the controlled human exposure studies that have been done over the last 13 years since the last ARB review do suggest both lung function effects and airway inflammatory effects at or about the current California standard.

DR. KLEINMAN: Thank you. I'd like to open this up to comments by the rest of the committee.

MS. WHITE: This is Mary White and this is really a question for my colleagues here. For a long time -- and it relates to are children more vulnerable than adults -- the conclusion about long-term effects, are we being more conservative than we need to be about the likelihood of long-term effects? Given what we understand about ozone and its effects, is it reasonable -- I'm interested in people's opinions -- is it really reasonable to think that there wouldn't be long-term effects on growth?

DR. TAGER: I guess, I mean, the answer would be -- I mean if you accept the animal toxicology models -- this is Ira Tager -- and particularly the intermittent exposure models and the airway remodeling, and even actually linking that with one acute study, the one by Gail Weiman in which it really showed much larger effects in the small airways, different kinetics than what is usually measured, and then the preliminary evidence from the study that John and I have done and that we're trying to replicate now, it certainly makes a pretty strong argument in that everything follows as it ought to. So I think we're being conservative because, at least when I saw the results -- and our study was almost

too good to be true and almost thought there must have been a mistake -- so I guess if we can replicate it in the study we're doing now in which we're also studying larger numbers and also linking it with some exposure studies to see who is actually responding and what kinds of responses, then I think we could remove some more of the uncertainty and perhaps make a stronger statement.

DR. BALMES: I agree exactly with what you said.

DR. KLEINMAN: Just as an aside on the threshold concept for ozone, ozone is one of those rare environmental pollutants that we do have a natural background of which strangely enough is right around the 30 ppb level. So it wouldn't be surprising that there is a decreased sensitivity below there. But when you put people in a chamber, superimposed on that you do see the short-term effects down and it doesn't look like there's any decrease below that -- which I guess -- I mean, it's sort of an obvious statement, but I don't think we necessarily conclude that if there are in fact chronic effects that they'll have the same shape. I mean, the cumulative effect may be quite different and it may not have -- it might have some completely different shape. The only point I was trying to make with the short-term data is that there's a remarkable correspondence

between studies of completely different types. I mean, cross sectional studies which people are generally very unhappy with, a natural experiment if you will, that is kids exercising on a treadmill, and then a modeling exercise from studies that were done over a broad range of exposures over a varying period of time, and it's pretty surprising if it's coincidence -- and I don't think it is -- that they come up with almost identical shapes, and that the area where the inflection points are not too far away from each other. And I actually know of some other data that's not been published in books similarly to that.

DR. WELLER: Barbara Weller. Hi. One issue that we haven't really discussed yet is the question of ozone responders and it is well known that there are a sub-population of the public that respond to lower levels of ozone than the general population. And there's some evidence now that there may be a genetic linkage there. So would anyone want to address that issue?

DR. BALMES: Well, having studied a fair number of individuals in the laboratory now with acute short-term ozone exposures, yes, there are impressive individual differences. I can use my wife and myself as an example. We both participated in some of my studies with exposures to

0.2 ppm for four hours. My wife has something like a 30-40 percent drop in FEV-1 and I actually am the least responsive of any person that's ever been in our lab with regard to ozone. I actually got slightly better lung function across that four-hour exposure -- perhaps an exercise effect. But I don't know what to do with that in terms of responding to what I thought was the mandate of our review because I don't know how one identifies those individuals. Maybe there will be some genetic tests in the future, but then that's also got a whole other separate set of issues about it. So I think we always have to be aware that when we look at mean data, either from epi or controlled human exposure studies, they're just that. And there are some individuals that have much greater responses. That's why I showed the figure from the E.P.A. report that showed that actually some individuals have 50 percent decrements in FEV-1 with a 6.6 hour exposure to 0.08 ppm, for example. So, yes, there definitely are differences that are quite profound. Usually a responder is reproducibly a responder and vice versa in my experience, and other people have looked at this.

DR. WELLER: I think it's just an issue that we might want to be aware of.

DR. BALMES: Absolutely.

DR. TAGER: I'd just like to make one comment and actually ask a question, but I think we ought to be clear about what the response is because the mechanistic response or FEV-1 really, which is FEC, well, it might be reproducible and fairly consistent among individuals, might be pathophysiologically unimportant or of secondary importance to inflammatory changes and changes in other parts of the airways. So the consistency of the inflammatory response, or the consistency of the response in other parts of the airways has not been as carefully -- I don't know how much data you have on repeat measures of inflammation with widely spaced exposures.

DR. BALMES: We actually have some now. And the acute inflammatory response, at least in terms of neutrophils, is actually reproducible in terms of widely separated exposures. Some people are responders and some people are not. And unfortunately, there's been no correlation and in fact sometimes even a negative correlation between the FEV-1 response and the inflammatory response. So you're absolutely right when you talk about responders, classically it's referred to symptoms and lung function drops of the FEV-1 type, which there's some correlation for, but if you look at airway inflammatory

responses, which may be more important in terms of chronic consequences, that's a completely different type of response.

DR. GONG: Henry Gong. Just as a comment to that question about gene environment interactions, actually in the U.S.E. Children's Level Health Study sponsored by the ARB, Dr. Gilling is actually looking at genotyping mucoceles, looking for specific markers for specific target enzymes that might take part in lung defenses. So that's one way of looking at this. That might spot some susceptible children to air pollution. And the other item also of importance is diet. And they're doing a very frequent -- it's actually called a "Food Frequency Questionnaire" on their children to look at various nutrients such as magnesium, vitamins E, C, and all that stuff. So the antioxidants may play a role. And I think in Jane's lab, they've also looked at this in ozone and sulphured oxide and see if they have a protective role. So that has something to do with who is susceptible and who isn't. There may be reversible things there too.

DR. BALMES: Again though, there are some important issues when one starts talking about genetic susceptibility to air pollution. You know, the Air Quality

Standards are supposed to protect the most sensitive members of the population, but when you start looking at genetic susceptibility, you do -- there are some ethical and some policy issues that haven't been grappled with heretofore.

DR. THURSTON: Mike, could I ask a question? I wanted to go back to something you said, Ira, that I was a little surprised, maybe shocked to hear you say, because I don't think you really meant it in as general a way as you said, that you didn't think there were more effects in children than there were in adults from ozone. And I think you may have just been talking about lung function decrements per ppb, but it came across as a broad statement.

DR. TAGER: Well, what I intended to say or what I intended was that to try to find evidence that children were more susceptible, meaning allowing for commonality of underlying disease, asthma or no asthma, level of exposure, activity, etc., that they were any more susceptible than an adult under similar circumstances, it would be difficult to ascertain from epidemiological studies.

DR. THURSTON: Okay, all right, maybe given that statement, but that statement is not true. The fact is that there is a much higher rate of asthma in children than adults --

DR. TAGER: That's not what I'm saying. I'm saying if you allow for a commonality of underlying susceptibility --

DR. THURSTON: Right, okay, that's why I want to clarify that because there isn't such a commonality. Children are outside much more, they have much higher rate of asthma and --

DR. TAGER: That's not what I'm saying.

DR. THURSTON: Well, I know, that's why I wanted to clarify it because I didn't think you were saying that, but you did say that without the qualifications.

DR. TAGER: Well, I'll make it unequivocal. Adjusting for all of those factors that obviously play upon exposure, I could not find any real evidence that children are more susceptible than adults. I'm not saying they're not, I just can't find convincing evidence of it.

DR. THURSTON: I think it might be worth talking a little bit about the factors that do make children more susceptible. One of the things -- obviously a higher rate of asthma, children with asthma much more effected than children not having asthma -- and the greater activity levels and -- one of the things that we have, and this isn't really fair because this is a paper that's being reviewed

right now -- but we looked in New York at ozone and PM effects in terms of hospital admissions and the basic premise of the study was to look at the effect of modification by race. And we did in fact find a higher relative risk for, well, a lower relative risk for let's say white, non-Hispanics than for all others for ozone and for PM. But interestingly, when you divided the data into those who were the poor and working poor vs. everybody else, all the effects were in the poor and the working poor. And you saw that within race as well. So once you corrected for that -- what appeared to be a racial difference -- wasn't there anymore. It was really a poverty healthcare difference. And of course, in America, children live in poverty at a much higher rate than any other age group. But I think those are all factors that are very important --

DR. TAGER: Yeah, but I think you're confusing -- I don't think we're disagreeing in the concept --

DR. THURSTON: No, I'm trying to elaborate on your --

DR. TAGER: Okay, but I think you've actually confused something that we need to be careful about. The fact that children -- there may be a higher frequency of asthma in childhood -- just means that there potentially is

a larger pool of people, allowing for the fact that asthmatics may be more susceptible. That's not the same thing as saying that a child asthmatic is more susceptible to the exposure. I mean, from a public health point of view, that obviously has implications. If there are a lot more kids with asthma, then the burden is greater in children. That's different than the issue of is there a unique susceptibility in childhood apart from the burden that they may carry with their asthma used as an example. And I'm simply saying, from epidemiological data and at least from what I can tell from reading exposure data, we don't know that. From a public health point of view, there's no argument that insofar as the burden of asthma may be greater in children, that also is a little bit difficult to ascertain given the way epidemiologic studies are done. There's a pretty considerable burden of asthma in older people too, particularly women. And so the public health burden aspect is not entirely clearly on the side of children as well, but I don't think we're fundamentally disagreeing.

DR. THURSTON: No, no, I think what you do is clarify something. But I do want to point out one thing -- this is something I brought actually talking about with PM,

but it fits into this too, which is that one of the things -- if I could put it up on the overhead -- one of the things that's been clearly identified is pre-existing respiratory problems put you at a higher risk. And you can see that -- I copied and pasted these numbers out of a report -- this is an overhead from current estimates from the National Health Interview Survey in 1996. I was actually trying to get this for 0-1 age group which I think would stand out even more, but if you look at this for under 5 years, this is the incidence of acute respiratory conditions per 100 persons, so it's corrected for population. And under 5 years, I think we all know this, but it's good to have hard numbers to look at, and if you look for under 5 years, you get 129 vs. for 65 and older, it's 49. So you're talking about almost triple the rate. So if you think of the elderly and they are a group that's at relatively high rates of health problems, but actually when you're talking about respiratory infections and respiratory conditions, under 5 -- and I think especially under 1 -- if we could get those numbers, I'd like to see them from California some time. I've been unable to get these numbers. We should dig them out. Now if you look all across the gamut, except maybe pneumonia where the elderly are just the same as under 5, but

generally they're a multiple of what the elderly are and well above all ages. So that's another way in which, since we know that air pollution more strongly affects people who have pre-existing disease rates --

DR. FRAMPTON: But these presumably are -- if I understand these presumably are acute infectious events in children, I mean, this is not news to me. Children have infections and, in fact, the New York Times indicates that you're probably better off having your kids get a lot more infections before age 2, it'll prevent asthma.

DR. KLEINMAN: George, I think this is getting to an area where we ought to solve this at dinner. Russ?

DR. SHERWIN: Yeah, Russ Sherwin. I have a different perspective on this. That inflammation you're talking about we see -- in respiratory bronchial -- is almost ubiquitously in our population. And we've been studying 14-27 year old sudden deaths from violence -- automobile accidents, homicide, that type of thing. So we virtually have 100 percent of everybody has got some kind of bronchiolar inflammation. And when you think about the fact that all you have to have -- if you have 15 percent of your lung inflamed, respiratory tissue, and all of it is in the proximal bronchial -- that is, the proximal centri-astor

[phonetic] region, you've got 100 percent impact on your lung function. And I think this may have a lot more to do with who gets abnormality, especially since one out of four of the young people we were looking at have what we call severe centri-astor inflammation, or proximal respiratory bronchiolitis. Where is that coming from? Well, that is what I think is the whole focus. It isn't a question of whether ozone does it, it's a question of all these things occurring in a population already injured. So the question is what role are those pollutants playing. Now one thing about ozone, the very basic lesion we look at -- the basic, not the severe lesion -- has been nicely reproduced -- elegantly -- at U.C. Davis at 0.15 ppm for three months in monkeys. This is precisely -- and they are of course much more sensitive than the mice we've been experimenting with, so we got down to .3. And very clearly, they got down to .15. This tells me -- I have no question that the lesion that I see is in part due to ozone. The only question is what's the magnitude? Is it high? Is it a major factor? Is it a major contributor? Or in combination with something else? But the big question is -- a big problem is -- there is injury. Ozone is playing some role, I'm sure PM-10 and 2-1/2 and nitrogen dioxide, despite the tendency to tone

down NO2, they are also playing roles. But the big thing is, I think, I want to make sure everybody knows my feelings that there is injury. This susceptibility is a problem in large part because you've got one out of four people already at a young age with severe illness. Those people ought to be more susceptible to your -- whatever tests you want to do, they are certainly going to be responders. And it's going to be very evident. So it isn't a question necessarily of pathophysiologic alterations of muscle. Oh, incidentally, I should also mention we did airway studies on these people. And in contrast to the dogma that says that asthma is associated with big submucosal glands and mucus hypertrophy, these kids have mucus gland loss. There hallmark is hypertrophic change and atrophy of glands. No wonder they have problems. We also see a lot of basement membrane thickening and even some aphelia [phonetic]. We're going to have a paper out shortly. I can't give you the data, but it's very high -- at least one out of four with very high counts of cyanophilous [phonetic] and basement membranes much beyond the 7 microbe [phonetic]. So this tells us that the old adage of not all that wheezes is asthma is extraordinarily true with the pathologic level because we don't see the usual signs of asthma in most of

these basement membrane ES cyanophile [phonetic], and inflammatory lesions of small airways.

DR. KLEINMAN: I guess one of the major problems, especially in evaluating young children, is that many of the things that we do for testing can't be done in the very young children. So we don't know if FEV-1 drops because we don't have very good measures of that.

DR. TAGER: But I think we know a few things from epidemiologic -- sorry, Ira Tager -- I think we know a few things from some epidemiological studies that have actually made measurements starting at very young ages and actually probably the best data from this are from the Tucson study in which they have a small set of children that they studied in the first couple of weeks of life and then were able to study again several years later. What they observed there has been observed in studies with adults, that lung function, your relative position in the distribution tracts very well. The kids who were relatively low when they're very young are relatively low as they grow up. So from a population point of view -- and obviously it doesn't hold one for one, but from a population perspective, one I think can say with a high level of confidence that if you look across a distribution of responses -- and let's take

pulmonary function -- the kids who are low to begin with are going to make up the bulk of the pool of at-risk people insofar as low lung function, relatively -- and I don't mean abnormal, I mean low in a distributional sense -- as they get older. And since we know that these low levels are predictive of a variety of morbidity, not just respiratory morbidity, they are a nonspecific marker for lots of other morbidity, I think we can be pretty confident that if we can study a five and six-year-old and know that child's relative distribution and get some idea of what their history was before, that we can probably on a population profile the risk of kids reasonably well.

DR. SHERWIN: Just a quick comment. Dr. Thurston made an interesting comment with that slide he put up showing high incidents of respiratory alterations in children and surprisingly one-third in adults. And I hadn't given too much thought to that, except speculatively. But when I started to show my material around, everybody agreed that I had substantial extraordinary inflammatory changes in the lungs of these young people, and they couldn't understand why they weren't seeing that. And the answer seems to be that they are looking mostly at older people. And when I look at older people, I don't see as much of that

inflammation either, but what I do see is they don't have much lung left. Now relatively speaking, it looks as though whatever was susceptible to inflammation injury is disappearing. There goes your FEV-1 decrement of lung depletion over time. And everybody -- all adults -- have some emphysema and I think the more resistant lung tissue holds on and we don't see that kind of acute information in large part because the susceptible tissue probably is gone.

DR. KLEINMAN: Henry or John, the Peters study -- the Children's Health Study -- had as one of its objectives to look at ozone in areas where there was high ozone, low ozone, and look at children's lung growth. Can you summarize what the outcomes are so far on that?

DR. GONG: Well, I can -- this is Dr. Gong -- I can quote the cross sectional data that was published last year, and I think it's summarized in Ira's section. Essentially, ozone dropped out as being a significant pollutant, whereas PM-10 and nitrogen dioxide and I believe it was nitric acid were the ones that were statistically significant for reducing lung function -- it depends on which outcome variable -- they were associated with symptoms and I can't remember about the lung function offhand, which ones.

DR. TAGER: They had cough too, I think.

DR. BALMES: Well, in terms of the lung function data from the cross sectional studies, and I think the unpublished longitudinal data also, does not suggest a strong ozone effect, but there is an ozone effect on respiratory illness absences from school. So when you're talking about measures of acute morbidity that actually cause kids to miss school, ozone was the dominant player. And also kids with asthma had more bronchitic symptoms in association with ozone. So ozone was not the main player with regard to declines of lung function relative to PM or NO2, but still was an important pollutant with regard to respiratory morbidity.

DR. GONG: Especially with asthma.

DR. BALMES: Especially with asthma, yeah.

DR. PRASAD: Shankar Prasad. A couple of things to follow-up on. Actually, that was paper we're getting published in the next few weeks. And from what I have heard and what was presented at the Board meetings, from John and the longitudinal section, ozone does not seem to be the primary predictor of decline in the lung function over period of time for a period. NO2, acid vapor and PM both cause and find continue to be showing primary significance

there. A question for John and a question for Ira Tager, you said about responders vs. non-responders. At that time, I recall you were trying to follow-up among the non-responders where the non-responders would be having a higher magnitude of inflammatory response. Do you see that as any -- that by what you are being a responder, the fume reduction itself would prevent an increased of ozone intake is what I'm referring to.

DR. BALMES: In one study that we did -- when I say "we," my laboratory at U.C.S.F., we did see a negative correlation between the FEV-1 drop and the amount of airway inflammation, suggesting that the individuals who changed their breathing patterns because they were symptomatic to ozone had a somewhat protective effect with regard to the airway inflammatory responses. And that's been seen in some other studies, so that may be true. There are other studies that haven't shown that kind of a negative relationship.

DR. PRASAD: Thanks. Dr. Tager, did I hear right from both of your overheads that you showed that you kind of hinted or indicated that in your opinion that the threshold may be around 40 ppb?

DR. TAGER: Well, I mean, if you look at the curve from Joel's paper, it looks very clear because it's really

all smoothed out. If you look at the data from Mexico City and Bill McDonald's modeling, it's somewhere between 40 and 70. The point I was trying to make is that the curve shapes are remarkably similar from different studies. I think Joel's data perhaps, just because of the way it's presented or was asked to be presented, without all the actual data in a smooth curve, make it look probably clearer than it is. But if you just lump those all together, all of those curves, and I drew them out with a pencil, so it wasn't exactly an elaborate analysis, it's somewhere between 40 and 70 that the shoulders were on the curve. And in an analysis that wasn't published that was done of the National Intercity Asthma Study -- and actually Kathleen Mortimer's paper on this is coming out, but it's not included -- this isn't included in the paper because there was a disagreement among the authors about whether it should be -- but we did a similar analysis and the shape of the ozone response curve was not dissimilar from what I showed you here.

DR. KLEINMAN: Great. We're going to take a ten-minute break. We're going to start promptly at 3:10. If there's a yellow sheet going around with requests for sign-up's for dinner tonight, you guys can deal with that and we'll be back at 3:10.

(Off the record.)

(Back on the record.)

DR. OSTRO: We were reminded to make sure you speak clearly into the microphone and if you cite a publication, to cite that clearly so it can be recorded in the transcript. So I think we're going to move on to NO2 now.

DR. KLEINMAN: Mike, before we get started, I just wanted to make a clarification on the restaurant invitation that was also to the people from E.P.A. and ARB if they would like to join us at the restaurant, whichever mysterious restaurant Bart has selected. So I just want to make sure -- the sign-up sheet is still over here, so you can get to it some time before dinner.

DR. LIPSETT: Okay, we're going to move on now to nitrogen dioxide, the current standard for which is 0.25 ppm, it's a one-hour average, and this standard, according to one of the former Department of Health Services long time physicians, told me it was initially set more on visibility concerns than health concerns. Nitrogen dioxide is kind of a reddish brown gas and it was set at this level apparently having something to do with visibility and the color of the air between the State Health Department Building in Berkeley

and the Golden Gate Bridge. Coincidentally, it also happens to be also a reasonable one, at least as far as we were concerned in the past for health protection. The standard is currently based largely on our analysis of controlled exposure studies with asthmatics, looking particularly at the outcome of increased bronchial hyper-responsiveness, not direct changes in lung function per se. And also on a couple of studies of patients with COPD which did look at changes in lung function. There have been several recent controlled exposure studies and, again, most of these are in Europe, that suggest that exposures to relatively low levels of nitrogen dioxide, including one at .26 ppm, averaged over one hour, may enhance the response of allergic asthmatics to subsequent challenge with air borne allergens. And basically this is almost at the level of the current standard. And since most children who have asthma also have an allergic component to it, about 85-90 percent of childhood asthmatics are also allergic, but that this interaction here might be something of concern for this population. Now, as with SO2 and as we're going to hear for particles tomorrow, there have been a number of studies that suggest effects on mortality, cardiac arrhythmias, asthmatic exacerbations, and a variety of respiratory symptoms. In a

number of these studies, as with SO2, there are problems of compounding by other pollutants. And it may be that NO2 has an independent effect, it may be that NO2 is an indicator of traffic. In any case, it is something that is related to high temperature combustion and the commonest source of at least population-based exposures in California is motor vehicle combustion. The children's health studies do seem to indicate that NO2, or possibly particles, or possibly acid vapors may affect lung growth in children, although this is not something where there's enough evidence to base a standard on at this point. And in general throughout California, the NO2 exposures do tend to be lower than the current standard, although occasionally there are excursions that are up to, and I think last year there was at least one, that exceeded the current standard. We put NO2 in Tier 1 largely because of the recent controlled exposure studies that suggest potential effects on asthmatics. And I think that overall the evidence for this is less strong than it is for particles and for ozone, but nevertheless, we felt that the evidence for this was stronger than for the pollutants that ended up being in Tier 2. So with that, I'll turn it over to Mike.

DR. KLEINMAN: Okay. I think I'd like to ask Mark

Frampton to comment on the review.

DR. FRAMPTON: Yeah, Mark Frampton speaking. I have a little to add. I think Mike did a nice job of reviewing the highlights. Just in terms of background, I think NO2 is receiving relatively little attention as a pollutant of concern in California and nationally simply because the interest over the last 10 or 15 years has shifted towards NO2 as an indoor pollutant because in a lot of homes, NO2 are sometimes a lot higher indoors than they are outdoors, and even there it's been hard to clearly demonstrate significant health effects. There's been a lot of conflicting epidemiologic studies and a lot of the older studies that looked at gas stoves vs. electric stoves failed to look at the fact that gas stoves generate ultra-fine particles and that what may have been measured as an indoor health effect was actually not NO2, but may have been particles or the combination. In human clinical studies over the years, our laboratory included, have been remarkably inconsistent in terms of the effects shown both in healthy people and in asthmatics, with older studies showing effects in asthmatics at levels as low as .1 ppm and yet others showing that asthmatics had no effects at levels as high as 4 or even 5 ppm. And the real reasons for these

discrepancies are not entirely understood, but the sense has been that it may not be as important as ozone or particles or other pollutants. In spite of this, as Mike mentioned, the thing that's happened in these numerous particle epidemiology studies looking at mortality and morbidity end points, every once in a while NO2 keeps popping up as sometimes the only pollutant that is significantly associated with some of these outcomes. In most of these studies, you can explain that away as NO2 as a marker of combustion and a statistical fluke, but not all of those studies. And there are some very well done studies that NO2 is the primary indicator or the primary positive indicator. And it's hard to exclude the fact that NO2 may be having a significant effect at outdoor levels, or at least having an effect in combination with particles or other pollutants. However, I do agree that I think the thing that is of most concern currently is these recent studies looking at the allergen response in asthmatics, and particularly the study, Michael, that you quoted by Strand and colleagues that showed effects at .26 ppm for half an hour. And these were exposures at rest of asthmatics who then went on to have an allergen challenge. So that is certainly below a level that I would have suspected there would be any effect. It's

certainly a level below which airway inflammation would be occurring in these individuals. And it's been observed now in probably three laboratories overseas at ranges from .26 to .4 ppm. I think there is need for confirmation of those studies in other laboratories and using other methodology. But it is consistent with some animal data that suggests that fairly low level of NO2 exposure may enhance some of the mechanisms of allergic responsiveness and it is consistent with the epidemiology that suggests that traffic related combustion products, including NO2, may enhance allergy in children. So I think it warrants some careful thought.

DR. KLEINMAN: Thank you. I'd like to open it up to comments from the committee. Henry?

DR. GONG: Mark, based on your very nice and complete review of the topic and my own experience with NO2 studies, do you think that NO2 should be in Tier 1? It seems like the flow of the information that we have is that it may be a surrogate, and you always qualify that, but nonetheless, that seems to be the primary message from your review. So we're sort of looking for something that it can do -- a gas with an effect. And it's hard to find one that really comes out at you as being clinically significant, and

significant for public health, I guess. So should it be in Tier 1 as suggested by the staff, do you think?

DR. FRAMPTON: Actually, I think it should be. And it's really for the reason that I mentioned and that Michael mentioned. If it wasn't for those human clinical studies of allergen exposure, then I would be hard put to justify putting it in Tier 1 because the epi data and the previous human clinical studies data is inconsistent enough that it's hard to really be convinced that exposures outdoors at this level could be having a direct clinical effect. However, with these studies, again, from more than one laboratory that are consistently demonstrating allergen responsiveness which would be a major issue for children, I think it does belong in Tier 1.

DR. GONG: This is Dr. Gong again. So I'll follow it up a little bit. You're saying based on uncertainty of its true health effects that we need to keep pursuing investigation of it, I guess, as well as putting it in Tier 1? Is that a safe summary?

DR. FRAMPTON: Yes.

DR. GONG: Could I also say what about sulphur dioxide, if I may digress? There we know that it's a strong broncho constrictor. It may not affect as many people, but

obviously there was concern expressed by Dr. Koenig about that.

DR. FRAMPTON: Yeah, I think in a sense, and this is a point we were talking about a little bit over the break, in a sense the larger extrapolation of your question can apply to any of these so-called criteria pollutants, and ozone in particular is -- do we really need to re-think our paradigm of standard setting? Really, as we get more able to detect health effects or physiologic effects of some of these pollutant exposures, it's going to be more and more difficult to say that we can rationally establish a standard for which none of these things occur for 95 or 99 percent of the population. And at some point, we have to begin to think about what are the important effects, the important effects that affect a lot of people, and what can we do about it. I don't have a good answer for that question. I think if your paradigm is that you've got to have a standard that doesn't have any effects, and has a margin of safety, then you should put SO2 in that category. But this has been kicked around for a long time with SO2, not just in California but nationally, and most people I think have agreed that the demonstration of short-term quickly reversible broncho constrictive effects probably is not as

significant or important a health effect as say late phase allergen responsiveness in allergic individuals, which has the implication of asthma exacerbation and effects lasting days or even weeks if they get sick from that kind of exposure. So I think we're talking about differences in degrees, but in terms of absolutes, I can't justify it.

DR. BALMES: So obviously a difference of opinion because Dr. Koenig said it will affect their lifestyle.

DR. FRAMPTON: And I agree with her entirely. I agree with her 100 percent. You can't say that that's not an important health effect. I think that it's just matters of degree.

DR. BALMES: John Balmes. Just one further comment about the NO2 enhancement of response to allergen. I mean, this is similar to what I was alluding to with regard to ozone. So it's important to point out that two oxidant pollutants seem to have the same effect, so that's I think stronger evidence that there actually is something going on here with regard to allergic asthmatics and exposures to these two pollutants. And I agree with Mark that it sort of raises my ante of concern for both pollutants.

DR. FRAMPTON: Yeah, that's a good point. The

interesting thing though -- the thing that's puzzling to me about NO2, with ozone, the studies suggest you need a concentration or exposure to ozone that's high enough to give you an inflammatory response in order to get the allergen enhancement, whereas these levels of ozone are way below the threshold for inflammatory response.

AUDIENCE: NO2.

DR. FRAMPTON: I'm sorry, ozone effect -- NO2, thank you.

DR. BALMES: I would in general agree with you except for the initial ozone study, the Molfino study, was at a level that wouldn't be expected to induce --

DR. FRAMPTON: Yeah, but that study was flawed.

DR. BALMES: They'll get a lot of other studies going, so it was useful. And then I would say that with regard to NO2, while there may not be BAL evidence -- bronchi alveolar lavage evidence -- of inflammation within an exposure at .25 ppm, several groups, I think probably including your own in terms of a bronchial wash where you're looking at more theoretically more proximal airways, and in our own studies with normal individuals at .25 ppm with a three-day exposure protocol, we did get some bronchial wash or more proximal airway inflammation, though not the BAL

information that you see with ozone. If proximal airway inflammation is involved in this response, then I think it is somewhat more plausible.

DR. FRAMPTON: That was with exercise though, I assume?

DR. BALMES: That was with exercise, yes, so it was a higher effective dose. But those were normals.

DR. DRECHSLER: Deborah Drechsler. So far we've only talked about NO2 effects on pulmonary and respiratory end points. There is a paper which it happens I wrote, but wasn't included in the review, that the subjects were older people, like 60's and 70's, and NO2 reduced -- when these people did light exercise, NO2 reduced the cardiac output increment that occurred due to the exercise. I don't think I'm explaining that well, but --

DR. FRAMPTON: Actually, I'm very familiar with that study and I'm surprised I left it out of the review, and I apologize for that.

DR. DRECHSLER: I'm not sure it's ever been repeated or anybody else ever even looked at it, and it was a pretty small group. But it is at least an indication that there may be effects on other organ systems beyond the lungs.

DR. FRAMPTON: Yeah, and I think that's a very good point. And in fact, our lab has some data also indicating there are systemic effects. It's not in the review because we haven't published it yet, but it's on my computer being written up. But we found a significant reduction actually in the hemoglobin and the hematocrit in the circulating blood in a dose response fashioned after exposure to NO2. However, the exposure levels were considerably higher than the standard. We're talking about .6 and 1.5 ppm exposures.

DR. SHERWIN: Yes. I wanted to mention that sometimes pilot studies or probes into amplification have potentially important meeting. My associate, Dr. Rictas [phonetic], published that, and it was mentioned in the review, the studies showing CE-4, CE-8 and other lymphocyte shifts much like you would see in AIDS, for example, so there was an alteration of the immune system at the standard level. Then also, which I thought was a very fascinating finding was that he would show more metastasis of most melanoma metastasis model by exposing the animals to NO2. So that carries with it the facilitation of metastasis in a patient with cancer which says, well, that certainly has some meaning. I wanted to raise another question, too, that

has to do with what happened to the .15 ppm 24-hour standard? I have seen times when the .15 was exceeded, but the .25 wasn't, and vice versa of course. So I wondered why that isn't a consideration. Then I'll just ask a couple other questions. Maybe they all can be answered. One is the importance of point sources -- for example, I work out at the club and the diesel buses all congregate there. And I keep thinking to myself, at one time before they had air conditioning, all of that diesel fuel came up and that's a tremendous amount of NOX. Now that they have air conditioning, maybe it's cooled and I don't get the effects as badly, but the big question I'd like to ask is, what do we say when we evaluate these standards of when we have to take into consideration that standing on that corner with three, four and five buses may give you a fairly high level of NOX on a point source basis. And I don't want to lose track of the standard difference, in other words one hour may not be as meaningful as a 24-hour, and that may not be as meaningful as maybe a week-long level. Any kind of comments on that?

DR. FRAMPTON: No. I agree with all of your concerns. I guess my concern when I jog on the road behind a diesel bus is not so much for NOX as it is for ultra-fine

particles, but you pick your pollutant and you take your risk, I guess.

DR. SHERWIN: Well, there's a lot of product particulates, but the NOX is one of the high emitters, there's no question of diesels.

DR. PRASAD: One comment. The issue of NO2 as an indicator or SO2 compounding, that's probably a commonality in almost any epidemiology. But when it comes to the question of PM, we tend to take a preferential -- a little more latitude than say it is primarily related to -- PM-10 is more than the others, so are we always stressing this issue in terms of SO2 and NO2, as opposed to the other times while we are evaluating PM?

DR. FRAMPTON: I don't know the answer to that. I think it's a good question. And I asked myself that question throughout the review -- without a good answer.

DR. THURSTON: This is George Thurston. Yeah, I was going to ask you about nitric acid, actually, sort of a related issue because Peter's paper finding associations in children's effects -- I think it was in morbidity -- you know, the California Children's Study -- with NO2 and nitric acid. And I'm wondering if those two things aren't linked and that maybe some of the variability that we see in NO2 is

sometimes you see NO2 with and sometimes without nitric acid. I mean, you know that NO2 goes in the lung and gets in the moisture and, as I recall, it turns to nitric acid in the lung. So nitric acid -- it comes up important in that study and what do you think is going on there? And then if we have time, I might respond to the particle preference.

DR. FRAMPTON: I don't know. And maybe John Balmes will comment a little bit, but the human clinical studies of nitric acid haven't shown much at all, whereas NO2 has been inconsistent. At least you can demonstrate some positive effects if you go to high enough levels and do enough subjects. So with nitric acid --

DR. THURSTON: Have you ever done nitric acid with particles? That's sort of answer to the question, really, is that I think, you know, when you look at SO2, you shouldn't look at it without particles. If you look at NO2, you shouldn't look at it without particles because it always is exposed with particles. And I think one of the reasons why particles comes out so consistently might be that it is this vector. It's not only a pollutant on its own, it's also a vector for other pollutants to ride the escalator down into the lung, whereas nitric acid would be scrubbed out readily, SO2 would be scrubbed out readily. If it

latches onto a particle, it's on for the ride and it gets into the lung, and it goes down and it's impacted. So I think that particles are sort of a double whammy in that they not only could have their own effects, but also can enhance the effects of other pollutants. And that might be why it comes out more consistent when you start doing multiple pollutant analyses with statistics, anyway. The particles generally win.

DR. FRAMPTON: And certainly, you're making a very good point that the issue is mixtures and we should probably be studying mixtures a lot more than we are. The problem is that -- I'm sure you're not arguing that we shouldn't study NO2 alone -- the problem is if we were to find that NO2 had basically no effects at the levels we're concerned about, and that it was all due to NO2 plus particles, then you're going to regulate the particles, and you need a particle standard and not an NO2 standard. So I think there is a need for studying NO2 alone and knowing whether NO2 by itself has effects from a regulatory and a mechanistic standpoint, but I agree with you 100 percent. And that's sort of the E.P.A.'s attempt to do this one atmosphere approach which I think hasn't gone very far. The problem is, at least in terms of human clinical studies, the

logistics of studying particle mixtures in any kind of informed fashion is very very difficult.

DR. PINKERTON: Kent Pinkerton. I'd like to also just emphasize the importance of especially studying more about the NO2, especially in terms of its response to allergens. Although we haven't studied NO2 at Davis, we have been looking at other oxidant gasses. And when you are dealing especially with the young child, and in our case we're dealing with young monkeys, that there's a tremendous effect of allergen combined with an oxidant gas on the development of the lung and on its remodeling and its eventual outcome as an organ for respiration. And it's all very adverse that we don't see in adults.

DR. KLEINMAN: We can open the floor to more comments if the committee hasn't got anything, or anybody from E.P.A. or ARB wish to comment? Then let's open the comments to the floor.

MS. MARTY: This is Melanie Marty. I had actually a couple comments, but I think I'll stick to the first one first. And this is with regard to this issue of intra-individual variability which, as a toxicologist dealing primarily with toxic air contaminants, we take that pretty seriously. In our risk assessment methodologies, we

routinely use an uncertainty factor of ten -- ten fold. So if we have a human study that we're working with to develop a reference exposure level which is supposed to be a safe exposure level, we will divide the no observed adverse effect level by ten to get to that referenced exposure level. Most of the time, we have much less less data than you guys have to work with on the criteria air pollutants, so ten may not be appropriate for things that impact at the site of exposure. There's lots of argument that ten might not be good enough for some chemicals, especially systemic toxicants where the toxic response involves metabolism, detoxification, excretion, all these other pharmacokinetics issues that come into play. Anyhow, really my point is that I think it's really important if you have data on sensitive sub-populations to attempt to quantify potential intra-individual variability in the human population and apply that when you're thinking about prioritizing, and also especially in the long run when you're actually developing a recommendation.

DR. BALMES: Melanie, I guess I don't disagree with you on a certain level, but if you're referring to ozone where we had some discussion about intra-individual variability, I mean, even if you went to a factor of three,

as opposed to a factor of ten, I mean, we might get ozone retainment in some future space and time, but again, I think it relates to -- if you're trying to talk about no health effects, given that we can demonstrate some subtle health effects at very low levels of exposure, if you then put a margin of safety of ten, three, on that, we're going to be down at the background level.

MS. WHITE: This is Mary White. I would appreciate a little clarification about the kind of levels that are currently being measured outdoors. You have a statement about the levels are lower than the current standard, but --

DR. KLEINMAN: For NO2?

MS. WHITE: For NO2, yeah.

DR. KLEINMAN: The one-hour standard is 250 ppb and the one-hour peak level, which has come down, is at about 175. So it's below it, but not --

DR. LIPSETT: And Mary, also on page 10 of the report of the Blue Book, the ARB put together some tables looking at the major air districts and the dates exceeding the different standards. And you see for NO2 generally, there was one exceedance last year which is in the South Coast air district with a one-hour level of .31 ppm, and the

other major districts had no exceedances. The mean levels were approximately, well, I guess about half of what the current standard is. No, this is the maximum, I'm sorry. The maximum levels were about half of the current standard in the other air districts besides South Coast.

DR. OSTRO: I'd like to ask the same question I did about SO2 regarding the findings from the epi studies. And I'm wondering, Mark, if you would comment on biological mechanisms for NO2 at the levels that we're observing outdoors and relating those to cardiovascular mortality and hospitalizations, what some of the epi studies are showing.

DR. FRAMPTON: I think it's entirely speculative at this point, except it's a little perhaps easier to make a case for it with NO2 than for SO2 because NO2, because it's a relatively insoluble gas and not as reactive as ozone, does penetrate to the alveolar region of the lung and can be expected to have effects in the deep lung. Again, there is not a lot of experimental data out there to suggest there are a lot of inflammatory effects at these kind of exposure levels, but as mentioned by Dr. Sherwin, there's some data -- there's animal data out there indicating there may be immune effects. And it is an oxidant. It interacts with the epithelial lining fluid and can generate lipid

peroxidation. It can produce methemoglobin and exposures in animals at somewhat higher levels, but not extremely high levels, that have shown formations of small amounts of methemoglobin in the blood following exposure to NO2, and that can affect oxygen delivery. So there are some potential linkages and mechanisms. Again, it would be hard to explain that at exposure levels below the standard. And there may be some mechanisms that we don't know about yet.

DR. KLEINMAN: I notice a dearth of comments and I thought this would be an opportune moment. Dr. Gong will not be able to be here tomorrow and he had some comments about PM. So perhaps, Henry, if you could take about 15 minutes?

DR. GONG: It probably won't take that long. Thank you, Mike. I apologize for not being here tomorrow, but at least I have a little time to talk about my opinion regarding the peership [phonetic] of PM. And based on my review of the documents provided to me and other experiences that I've had, I think that currently PM should probably be the number 1 pollutant on Tier 1, if you had to prioritize them. Owing to the fact that we know a lot about it epidemiologically, but we still need to have more information about its mechanism and even extra pulmonary

effects, as was mentioned already, and of all the pollutants that we have discussed or will be discussing, with exception, I believe, of hydrogen sulfide, I think that this pollutant has very little clinical information regarding its effects on children or infants. There is some data, obviously, on infant mortality, etc., but I think this is certainly an area that we need more answers and more research to provide those answers to help us understand its public health effect. And that's sort of a general statement that I have.

DR. KLEINMAN: Okay. Are there any responses to that general statement anybody would care to make? Any disagreement? Should it be in Tier 2?

DR. PRASAD: With the information that we have, do you think that is more than what it is for the ozone?

DR. GONG: That is more than what?

DR. PRASAD: What the information is available on ozone?

DR. GONG: Do we have more information on it than --

DR. PRASAD: Yeah. Do you think that in your opinion that between the ozone and the PM that the information on PM is much more than what's available on

ozone?

DR. GONG: No.

DR. PRASAD: I mean, to immunity. I mean, in order to prioritize between the PM and ozone, you are comfortable to say that the information available to review the inadequacy of the PM is more than what's available to review the inadequacy of the ozone standard?

DR. GONG: Well I think it sort of applies back to the nitrogen dioxide. It's really the uncertainty. We don't have all the answers and yet there's been a lot of epidemiological evidence to indicate its association with health outcomes -- adverse health outcomes. And that's the part that concerns me and I think that until we know otherwise, we have to pursue that vigorously, I think.

DR. PINKERTON: Kent Pinkerton. I would agree with Henry's comments too, but I'd also like to make the comment that I don't think ozone is a past issue. I mean, we still have to deal with that. And although PM has taken the front seat at the moment, and I think rightfully so that it should be there because I think we know less about the effects of PM than we do about ozone. But in terms of considering their priorities, I wouldn't say that PM is going to be something that should make us forget about

ozone. DR. PRASAD: I just want to add that just now you said that there's more uncertainty about PM than on ozone. If we know less on PM, we should try to know more on ozone, but we should try to know more on PM. Does it mean that that gets a priority for the standard review, knowing that the information available could be less than what's available for ozone?

DR. GONG: But doesn't the review that you're talking about take place within the next one to two years --

DR. PRASAD: Two years, period.

DR. GONG: And as you know, there's a lot of research being done on clinical mechanistic, even epidemiological aspects of PM. And these answers will be hopefully rolling in to help us do a better job of evaluation, understanding and writing reports and coming up with more supportable types of regulations.

DR. FRAMPTON: Maybe I could interject a thought here -- Mark Frampton -- it sounds like maybe we're confusing two things. One is sort of research priority, and the other is sort of priority for review with regard to the California standard setting process. And the orders of priority may be slightly different for those two issues. And I think that PM in my mind probably certainly gets the

priority for research needs. And I think everybody would agree with that. I'm a little hesitant to say that it gets the priority for review and in part that depends on how urgent we feel that the standard might need to be changed for particles because particles have been reviewed up the wazoo in the last few years and ozone perhaps less so, at least at a national level. So I guess what I would suggest is that we try to keep separate the idea of research needs vs. urgency of review for the standard.

DR. KLEINMAN: I think though, in the context of this particular process, it's a review of the standard with respect to protection of children and not the general review which, I agree, has been done quite well. So I think that's a slightly embellished issue.

DR. BALMES: So taking your point, Mark -- this is John Balmes -- taking your point that the review of the adequacy of the current California standards is somewhat separate from research needs and focusing on children, then I think you can make a good case that ozone is actually more important than PM for regulatory review. There certainly are very compelling reasons why PM might need to be controlled more if you deal with adult responses and specifically mortality. But I think we do know more about

responses of kids to ozone than we do in terms of PM responses. And so separating the two in terms of research needs vs. review of the adequacy of the current air quality standards, while I think PM should be reviewed, I think you could make a case for ozone being the number one Tier 1 pollutant.

DR. KLEINMAN: It may be premature to really argue the issue of primacy of PM vs. ozone since we haven't really sat down and listened to the entire discussion of PM which we will do tomorrow. So maybe we ought to hold off on that discussion, although I'm glad you had your chance to make your point because you're not going to be here tomorrow, I guess. Or are you?

DR. BALMES: I will only miss part of tomorrow.

DR. KLEINMAN: Good. Okay, then what I'd like to do -- let's open the floor to comments on all of the pollutants that we discussed this morning. I understand that there are some public statements that are coming due, so we have time for those now.

MR. HEUSS: My name is John Heuss and I'm with Air Improvement Resource, Incorporated. And I and Dr. Jaroslav Vostal are gong to be speaking today. And we're both representing General Motors Corporation. I'd like to spend

my time talking basically about ozone and PM issues, intertwining the two. I do have some copies of the essence of what I'm saying that can be provided to the committee. One of the factors listed in the draft was concerning the degree of exposure relative to the level of the standard, and I guess as I read through the document, I was concerned that this was not really adequately provided. The significant background of ozone that Dr. Kleinman mentioned was not mentioned at all. Other issues about the levels of the standards in California were talked about in very general terms, but I think there's some key issues that I'd like to bring up related to that. And the document didn't discuss what human exposures will be when the California state standards are achieved. I'd like to start with a little discussion of the sources of ozone. Obviously, we've been talking primarily today about the photochemistry of man made emissions, but there are other sources. Ozone in the stratosphere does mix into the Troposphere and is lost at the ground. There's another set of photochemical reactions occurring involving geogenic and biogenic emissions. And these involve things like methane, isoprene, turbines and metrol NOX. There are also issues related to transport. And here the transport is not only the transport of manmade

emissions from major source areas out into rural and remote areas, but there's also a phenomenon called the Tropopause folding event where plumes of high level ozone is inserted into the troposphere, generally at elevation where it mixes over a period of time into the rest of the troposphere. Unfortunately, that mixing generally occurs on the back side of high pressure systems, which is also the place where manmade ozone accumulates. These plumes have been found on very rare occasion to get down to ground level, but concentrations of up to .20 ppm are higher. This background does average about 0.04 ppm. It's a little higher in the spring and a little lower in the fall, but it is not just a constant. There are yearly peaks that range up to 0.07 or 0.08 ppm. In fact, if you look in the ARB databases, the locations that have the least emissions and the cleanest areas within California do typically get up to this 0.75 to 0.85 once per year concentrations. The state standard is .09 for one hour and it's again a once-per-year kind of value. This means that on days when there is a substantial background above .04, that the margin for man-made ozone is only the order of .01 or .02 ppm. We think the presence of this substantial background needs to be taken into account in any decision regarding revising the California standard.

And if you're going to go ahead and re-look at the California standard, we think you need to initiate detailed field studies of ozone levels in sources in remote California locations to try to decide how clean you can possibly get. And when this standard was set back in 1987, the staff assumed that the ozone background did not exceed .04 and it actually does. So PM-10 for the 24-hour standard, the state standard, is exceeded throughout the state except for compliance in a few high elevation counties. In fact, except for Lake County, the other basins routinely exceed the 24-hour standard. In the great basin valleys, the maximum has been the order of 400 microgram indicated in recent years. Now in contrast, the annual geometric mean levels do attain the state standard in the rural and remote areas, but exceeded in the more populated air basins. Or even in the rural remote areas, the geometric mean varies between 20 and 30 micrograms, so there's not a lot of cushion even there. It's well known that wind-blown dust is a major contributor to this and crustal materials -- some of that is controllable and some is not. The important thing here for California is that the levels of PM-10 that can be achievable will vary significantly throughout the state. And also, the

composition of that PM-10 varies significantly across the state. And that composition difference may alter the toxic potential of PM-10. And these variations I think need also to be taken into account when you talk about revising the standard. Another issue that I think is important when you start looking at extra human exposures is indoor/outdoor relationships. And Section 3.6 of the draft needs to get into a little more detail some of the material that's included, but also in the document, about comparison of indoor and outdoor. A recent study actually carried out in homes in Upland and I think Lake Arrowhead Township, which was published by a Harvard group, showed that ozone indoor/outdoor ratios with air-conditioning in use were about 0.1. Now when the windows are open and the air conditioning is off, there's clearly much more ventilation and ozone is higher, but it still seems to be lower indoors at .68 compared to the outdoors. Now for PM, indoor/outdoor ratio is often greater than 0.1, and in some recent studies it's shown that it's more like 1.5. But it can vary between .6 and 2 and 3 and 4. And there are a lot of studies of PM exposure coming on now because of some of the things mentioned. The research community has gotten into this in some detail. And one of the things that's coming out there

is, as you get more detailed real time measurements, you find that there are some significant short term exposures to ultrafines, fines, and coarse PM with the kind of daily activities we all undergo. Another of the five factors that the draft listed was the level of risk effects anticipated at or near the existing standard. And so I'd like to talk about both ozone and then PM. When E.P.A. last reviewed the federal ozone standard in 1997, they made a decision. And as they built up to that probablistic risk assessment that Dr. Vostal is going to discuss in a few minutes, it played a key role. And you're also, I'm sure, all familiar with E.P.A.'s Clean Air Science Advisory Committee. They looked at the results of that risk assessment and decided that there really was no bright line distinguishing any of the proposed standards as being significantly more protective of health. And those standards considered the current one-hour federal standard down to levels that were roughly equivalent to the current California standards. Now E.P.A. did promulgate an eight-hour standard, and I'm sure most of you are aware that that standard has been challenged and is now being remanded back to the agency and the whole issue is going to the Supreme Court. But I think you need to understand why. E.P.A. was unable to categorically defend

its choice to the Court of Appeals. The Court of Appeals noted that E.P.A. regards ozone definitely and PM likely as non-threshold pollutants, that is, ones that have some possibility of some adverse health effect, however slight, at any exposure level of below zero. The Court indicated, therefore, the only concentration that's utterly risk free would be zero. And for E.P.A. to pick any non-zero level must explain the degree of non-perfection permitted. And the Court found that E.P.A. articulated no intelligent principle in applying the factors to the databases that are available to choose those levels.

DR. KLEINMAN: Excuse me, John, I do want to allow time for other people to participate and what I'd like to do is ask you to kind of cut to the chase for this particular venue, which is to look at which pollutants should be reviewed first with respect to whether they're protective of children, not whether we have standards at all, because that's not what we're dealing with. This is just a matter of prioritizing at this point. So if you can kind of focus on our issue, that would really be helpful.

MR. HEUSS: Sure. I guess I'd like to talk a little bit about PM risk issues as I developed my last slide. Obviously, ambient personal PM is a complex mixture

with unusually large uncertainties because you're not dealing with individual components as the other compounds that you're talking about today. And we're all aware of the many health hypotheses involved. And as we try to understand this, I'd agree with the comments made earlier that we really want to focus our activities particularly for PM, identifying which components are causally related to health effects. And so you really need to, not only for children, but for everybody, to try to understand what is happening not only in an association sense because there's literally thousands of studies now that have attempted associations, and literally hundreds that are published of various kinds. And to try to work through all that to figure out what's really going on to understand the issue so that the kind of controls that are applied beyond the ones that are already in place and will be occurring are focused on things that will definitely help children's health and others. And I guess for ozone, we want to point out that the existing standard is very close to background. It's amazingly close to background. And any tightening of the standard based on the probablistic risk assessment already done by E.P.A., and with that result, the significant reduction in risk to children or others. And I think for

NO2, we feel that the case for first Tier reviews, again because the NO2 levels are considerably below the levels that have been raised as possible concern so far, the focus there ought to be doing the research to find out of there is a major concern related to the asthmatic children or not, and then decide whether or not if there is, to go ahead with the review of the standard.

DR. KLEINMAN: Thank you very much. Are there any other public comments? George?

DR. BALMES: Can I just make a comment on that because I noticed there were no references provided. My knowledge of the effect of air conditioning on ozone levels does not agree with the numbers presented there. I think if you look at Weshler, it was in the ALMA Journal about ten years ago, it's more like .5, but just off the top of my head, but you don't give any references. Also the background that you present includes --

MR. HEUSS: I'll be glad to prepare -- give you the references.

DR. BALMES: Yeah, that would be helpful to have references. Also, the background that you cite, if I'm not mistaken, includes man-made background, so that as you were to meet the standards in urban areas, that background would

also go down.

MR. HEUSS: The background I talked about is from the stratosphere and the geogenic and biogenic emissions. It's the lowest concentrations I've observed anywhere -- not the lowest anywhere because ozone can be significantly below the 40 ppb under certain conditions. The issue I was trying to raise is that these tropopause folding events do insert high levels of ozone. A recent paper by the Knoll Group with aircraft flights showed quite consistently very high levels of ozone in certain areas in the troposphere associated with extremely low CO concentrations, indicating stratospheric source, and that these concentrations, based on studies that were done in the 70's and 80's do insert into elevated layers, do mix down and provide a background that occasionally gets over .04 ppm. And that's the issue.

DR. LIPSETT: Could I -- this is Michael Lipsett -- could I ask, actually not you, but if any of the ARB staff were here, if you wanted to comment about this issue about the stratospheric intrusions into the troposphere here? Because we rely on you for those assessments as to what background levels are in California.

MR. CROES: Hello, this is Bart Croes. We're certainly aware of the research done on tropospheric folding

in the Eastern U.S. We have not done a comprehensive study here in California, but the data that we have looked at from our field studies and from background ozone monitors offshore indicate that the global background that we see is .04 with no -- and every excursion about the .04 level appears to be associated with transport from urban areas.

MR. HEUSS: I'll be glad to provide a couple references which indicate that this other phenomenon does occur and does get involved. In the past there have been a few studies in the Western U.S. too.

DR. LIPSETT: Yeah, if you have references for the studies done in California, that would be very useful.

MR. HEUSS: We'll provide that for the committee.

DR. KLEINMAN: Okay. Were there any other comments? Dr. Vostal? Can we do this in about ten minutes?

DR. VOSTAL: Oh, I think so. Since we have extra time for -- it depends how many questions.

DR. KLEINMAN: Well, that's why -- I wanted to leave time for questions.

DR. VOSTAL: Yes, now, certainly. That's the important thing. Maybe tomorrow there is another period of time reserved for the PM, so maybe I will start to just to continue what you have heard already. And this is really

something about the fact that although we are likely to say that this -- at least I personally -- that we have to commend the ARB staff and OEHHA for preparing very excellent reviews of the issues. But in spite of the fact that they are very thorough, there might be still some areas where we can redefine that something was in literature which seems to be very important and maybe it should be brought up. One of the facts is how should we evaluate the exposure. If it is accepted, first of all, that the children are spending more time outdoors, there are some studies that they might not always be the same type of the ratios of the time, as we can find in Wiley and Jenkins [phonetic] and so on. For example, there was a study by Hockney and Lennon [phonetic], the ones that they really have been showing that, surprisingly, not all the California children are really spending all the time. But what is more important is that if they are spending the time outdoors, are they really exposed to ozone? So let me just take a look at how can we evaluate this type of the exposure. The first thing which is important to keep in mind, and this is where it all started, with doing the relevant exposures with relatively heavy exercise, is that when you are exposing adult people, then at first they tolerate without any indication of any

measurable, you know, clinical effect, that they can tolerate levels as high as .5 ppm, and they can tolerate levels which are much higher than when we are talking about anything what it is. But particularly, what we have come to is that if we are concerned about the exposure -- exposure in adult people and also in children -- we have to really consider that there are really more than one aspect of the exposure measurements. Up to about the year 1990, E.P.A. is really evaluating that all the people who are residing in areas which are not in compliance with the standard are exposed to ozone. And they were agreeing [presumed] that this made a very profound impact on the human health -- on the public health. But now when you look into it, ozone, particularly in California, is not really extending exposure for the whole day. There is nothing in the night and when it starts in the morning it goes and reaches a maximum, and then it disappears slowly. It is also moved depending on the prevailing winds and so on. So particularly what we have to postulate is that you must be exercising when ozone concentration is high, you must be there at the time when the concentration is high. You must be outdoors. And we know that the people are spending most of the time indoors and so on. And you have to be exercising. So practically

when we are [inaudible] since they are independent from [inaudible], each one is a factor in which you can determine [inaudible]. And when you are multiplying the perimeters, we are coming to much lower levels of potentially exposed people than it has ever considered. For example, when we started to discuss it with E.P.A., then ultimately, as you can see, it was in 1990 that about 62 million people who were claiming that they are exposed, and we started to really apply this type of the deterministic approach, it came to much lower numbers. But what is even much more important is finally E.P.A. rejected the original deterministic approach, and they have built up a model, it was called PNAM, [inaudible] National Ambient [inaudible] model. And it has been used. And the data which were published in -- not published, they were released -- from the OAPS [phonetic] in 1993 and 1994 are showing very clearly that what you are seeing here is that when you compare the conditions as they were in 1991 -- and I'm quoting here the E.P.A. data -- then there might be still some significant fractions of the children exposed. But when it comes to the point when the E.P.A. has credited that whether the standard will be an attainment, and even in Los Angeles you can see how smog has evened out the fraction of

the children which will be exposed. So that means how important are those new numbers. And therefore, the studies which are really taken and published in the report, some which are talking about some type of the [inaudible] exposure, ultimately just based on the fact that the people were residing in the area where you have some violation of the standard or elevated ozone levels, it doesn't really mean that those people have been really exposed to ozone, and therefore maybe we should not be making it such a fear. Now this is --

DR. LIPSETT: Excuse me. This is Michael Lipsett. Could I ask a question about that last graphic there? It looks like those calculations were done using .12 ppm, the old standard? And how much would that change, if at all, if one were looking at more extended exposures that would be, say, consistent with the results of the E.P.A. controlled exposure studies looking at .08, .10, this sort of thing?

DR. VOSTAL: First of all, as you can see, when they [inaudible] what can we really estimate what were the potential contacts for people with some type of the concentration of the ozone which seems to be producing some measurable [inaudible]. It has been taken from the original exposures, original data by [inaudible], and they have

estimated that it should really be some type of exposure which was defined as what are the one-hour standard -- that exceeded at least for one hour -- you can really just come to the violation. [Inaudible] rate of the [inaudible]. So this was previously done before and it [inaudible] from exposures as we feel [inaudible]. What is even much more important is this was really based on the fact that the only one measure which we have had at that time, was it really really thought that if you want to measure the effect of the ozone, would it be best measured [inaudible]. And the [inaudible] surprisingly just been shown. I've heard it here many times in the morning, it seems, that the children are maybe showing -- maybe asthmatic children -- will be showing some larger sensitivity to ozone exposures. [Inaudible] maybe 15 years ago, E.P.A. teams have shown that when they compared asthmatic people with normal healthy volunteers, they have not seen any type of response in the asthmatics. The explanation was that probably the dose exposures when the asthmatics have really large levels of the mucus in [inaudible], then they weren't functioning as some type of a [inaudible] and therefore needed [inaudible]. Yes?

DR. BALMES: Are you saying that there were no

responses on the part of asthmatics?

DR. VOSTAL: No, that there were no different responses.

DR. BALMES: No different, well, that's a -- and I think that's generally considered to be true for lower level of exposures. So I agree with you. I just wanted to be clear that you --

DR. THURSTON: For that outcome. I mean, someone who doesn't have asthma is not going to have an asthma attack, right? So if you compare a non-asthmatic response to ozone vs. a child with asthma who will have a higher chance of having an asthma attack, that's quite a difference. That's what we're talking about. We're not talking about differences in lung function. We're talking about having an asthma attack vs. not having an asthma attack. That's quite a difference between children who have asthma and don't, or vs. an adult who is less likely to have asthma than a child.

DR. VOSTAL: George, I have to disappoint you. We don't have too much of the evidence, if at all, in this maybe, that you can produce by the inhalation of ozone a typical asthmatic attack. You can produce it by inhalation of SO2 without any question. You know, everything has been

measured for SO2 --

DR. THURSTON: Oh, I could refer you to epidemiology. Chamber tests of just ozone alone -- and of course then you don't get the interaction with other --

DR. VOSTAL: Oh, certainly. On the other hand, I have really to say that if you really are looking on it, that there might be some interactions with other factors. You have to realize that there are so many factors that the epidemiology cannot always distinguish what is the causality and which one of those factors is causal. So I suppose that this is really a question which is open on both sides. But let me finish, first of all, I saw what is even more important what has happened is -- in 1995, there was a meeting in Honolulu. And there was a paper presented and I'm sorry that it has not been mentioned in the excellent reviews, whatever you have in here, where the same group which started the concern about the ozone impact on the forced respiratory volume, that means Hazlekrat [phonetic], Bromberg, Bates, and all the other things, have really done an experiment which is crucial for our understanding about the question of adverse health effects due to the ozone. If you really see it here, those were volunteers who were exposed to about .14 ppm of ozone while exercising. And

they have really done it in two different rates. They exposed it in there at infusion of say -- that they have taken the Sufentanil. Sufentanil is honestly the agent which is being used for the analgesia for the higher doses for analgesic effects in lower dosages. This was the lowest dose infused immediately after the exposure. If you really see in the lower [inaudible], if there was the saline infused, there was a significant [inaudible] involved in femurs and in mares [phonetic], but where [inaudible] that there was practically no response at all. And therefore [inaudible] that what we have been originally thinking about that it could really be an effect of some injury done to the respiratory airways, it is not an injury. It is simple refractory measures.

DR. KLEINMAN: Excuse me, it says there in the post-exposure FEV-1 that the FEV for males and females after ozone dropped exactly the same as in the previous one, and you're reversing it with a drug. But we can do that with lots of bronchodilator and things like that. I don't understand the significance of giving a drug after the exposure.

DR. VOSTAL: The significant issue that the forced respiratory [inaudible] that's never been developed for

measuring changes in pulmonary functions of some temporary transient character. The force respiratory volume has been talked about to measure mainly what is the possible handicap of people [inaudible] that they cannot really make enough of the respiratory/post-respiratory volume. It has been therefore here where we are seeing it and particularly all the experience which you have shown in here always show that there is a transient effect and that [inaudible].

DR. KLEINMAN: Yeah, but some asthma attacks are transient too, and you can reverse those with bronchodilator. John?

DR. BALMES: I guess, I mean, I don't disagree with you that with or without a Sufentanil study, which I was vaguely aware of, but I hadn't seen the actual data, the FEV-1 responses to ozone are transient responses they're generally reversed, well, within 24 hours -- I shouldn't say "generally," -- usually reversed within 24 hours of the exposure. That's one set of responses to ozone. And I would beg to differ with you with regard to the usefulness of FEV-1 for transient responses of the respiratory tract. It's still the best measurement of that, as well as being a good measurement of chronic impairment, just to be -- I think to be proper about the physiological importance of

FEV-1, it's both a measure of acute responses and chronic responses. But while the 1987 review -- the California standard -- was based on these FEV-1 responses, it's not the only response to ozone.

DR. VOSTAL: Let me just read it for you. The only one which I fear -- in this paper -- and I am not defending it just as my paper, it is paper which was done by the team. In 1973, they referenced [inaudible] that it was on exposures, you know, decreases in FEV-1 performance. Now they didn't know how to explain it at the time, but they were smart enough, and if you look into the paper, it was [inaudible] -- at that time, they said there is a possibility, since we have found over the same time, reduced function of capacity of [inaudible] that this is due to the fact that those people cannot take the same deep breath to really produce the same type of the effects as they have done before. And now when the Sufentanil was there, that it indicates that this is simple, you know, refractory, not many agents, you know, top of the persons and not as originally [inaudible] as a temporary intransigent damage to the respiratory [inaudible].

DR. KLEINMAN: Just to reiterate, I think, Vostal, that the fact that it reverses with Sufentanil does not mean

that there's not an airway injury going on. In fact, we know there is airway injury going on, there is elaboration of Substance P which mediates this neurogenic effect, and there's airway inflammation.

DR. VOSTAL: That's a very good point. I suppose that this is really coming back to the point that maybe you as an advisory committee have to return to the point of how to really define when we are talking about the adverse effect. Now there is no question that there have been some [inaudible] identified. There is no question that you can find, as we can really discuss further on, some type of [inaudible] of the cells which are normally not in the same concentration, and so on. But the point is that to really talk about the injury, and if you really are saying that if this recovered from it maybe within a few hours after the exposure, it's very difficult to accept that this is really an adverse effect, which means there was damage to the whole system. So I think that from this point of view, what I feel is important is at least [inaudible] this review of the standards should at least review the paper. The paper has been published now in 1998. And everyone can find it there. And I suppose that they are discussing the role of the C Fibers in [inaudible] this type of response. And all what I

read here [inaudible] that there is some type of injuries. Now when it comes to the injury, maybe we should really be talking about what are the so-called inflammatory --

DR. KLEINMAN: Jaro, we're going to need to get to the final issue.

DR. VOSTAL: This is the end. It is the same discussion -- what do we call as an inflammatory process. And if you really listen to those people who started -- Wright [phonetic] and Korin, and so on -- the only comparison which is claiming that there is an inflammation is that we are able to measure the presence of some [inaudible] before and after, and we can measure even some distinct increases under the exposure. The point is that the increases are [inaudible] very small. And Korin presented it for the first time that he was using some rapid comparison like 200 person increase and 400 person increase. But if you look into the [inaudible], you find an increase [inaudible] from half a person of a cell to two person [inaudible].

DR. BALMES: That's actually a misstatement of the data. I know these data very well. I've contributed to them. And actually the usual number of neutrophils is two percent or below, and at the .4 ppm level that Hillel Korn

[phonetic] first used in 1989, they had -- it went to ten or 15 percent, so it's not from .5 --

DR. VOSTAL: No, I [inaudible] that it wasn't decreased from .5 to 2 or something. And if you look into it, then you have found high levels of --

DR. BALMES: It went from .5 to like 15 percent.

DR. VOSTAL: [Inaudible] from the data. Not everything we can change should really be declared that this is really very significant. It is the same rate as [inaudible], for example the total blood count of the white cells and how much it would really be changed during the data and so on, we are taking the indication of an [inaudible] only after it is extremely high. And therefore it may be that we should talk more about the physiological defense rather than [inaudible]. That's all that I wanted to say.

DR. KLEINMAN: Thank you very much, Jaro. Are there other comments from the floor regarding the other pollutants that were discussed, or the way in which the pollutants are currently being left in Tiers? So Tier 1 is currently PM, Ozone and NO2, with the others being in Tier 2, which just means that it relates to when they get reviewed, not whether they get reviewed or not. Mary?

DR. WHITE: Yeah, this is Mary White. I had a question just about the process. I looks like the first pollutant is going to be reviewed for two years and any pollutant after that only for one year. Is that correct?

DR. LIPSETT: That's the legislative timetable that's been set up. And in the past, I mean, pollutants like PM and ozone that have huge databases usually take at least a year and a half to two years to do. So probably the way it'll work in practice is that there will be an overlap. But we'll start reviewing PM and the next one will be started maybe half way through the PM process.

DR. BALMES: Could I just ask the representatives from GM whether they have a preference for PM or ozone in terms of Tier 1 reviews?

?: First of all, we are not representatives of GM.

DR. BALMES: John said he was a representative and that you were as well, so I'm just --

MR. HEUSS: We are on behalf of GM, but we're representing ourselves.

DR. BALMES: Okay, so then on behalf of GM, representing yourselves, do you have any feelings about whether ozone or PM should be tackled first?

DR. LIPSETT: And actually, can you speak into the microphone for the Court Reporter, please? Thank you. And one other thing, Rachel is reminding me that everybody has to be out of here by 5:00, so we have to have time for closing remarks by Dr. Kleiman as well.

MR. HEUSS: Sure. The written materials I provided you copies with has at the end a list of recommendations. We recognize the PM issue as such a wide burning issue that, with all the things going on with excess funds being put into that for a number of years, the National Academy of Sciences and others, it's clearly something that needs to be understood and you all ought to be looking at that. We don't think ozone because of the fact that you have an ozone standard that's significantly more stringent than even the new ADAR E.P.A. standard and is very close to the background. When you get done with that review, you won't be able to do anything to make that lower and still get it achieved anywhere in California, which is our hope one thing you'd like to do. So that's the basic bottom line. I did provide two papers to Rachel, one on ozone in residences and the other about background ozone that I asked to be provided to the committee. Thank you.

DR. BALMES: Thanks.

DR. KLEINMAN: It looks like there are no other comments, at least no one raising their hand. What I'd like to do first is thank everyone for the considered remarks and the presentations. And we've looked at the first three of these pollutants -- well, four actually -- which are extremely important. Tomorrow we'll be dealing with several others. And then we will have additional time for public discussion and especially looking at the prioritization. There were some questions raised about -- and this is more for the committee to consider in terms of our discussions for tomorrow -- for example, the issue for sulfur dioxide of how to utilize the mouthpiece exposure data, whether it should be given equal weight with the oral/nasal data or not in terms of using those levels as part of a standard setting process. Also, to what extent is SO2 a surrogate? But that might be asked of any of the audience. I think an overarching issue that keeps coming up is the issue of mixtures. And at the present time, there's really no good mechanism in place for thinking about the role of these pollutants as part of mixtures. And in the reports, where it was possible to do so, there were sections on interactions. And I believe that should be covered. Russ, you have a comment.

DR. SHERWIN: In view of the fact that some people will be going, there's comment I'd like to make and have to think about it. I don't know whether we have time to respond. But I wanted to mention that the PM-10 is not strictly a micron measurement. And some people are not fully aware that we have found well over 35 micron particulate particles -- platy fibersilicate -- platy and fibrous silicates in lungs of humans. So I just want to point out that the PM-10, the PM-2.5 is your mass medium aerodynamically equivalent in diameter which has nothing to do with pathology. But if I was to look at a human lung, I can find particulates in the alveoli which measure 35, 37 micra, and not the noxious fibers that we worry about, especially asbestos, all are important when they're over 10 micra. Twenty to 40 micra is the average size of the ones we get and I see 350 micra asbestos fibers in the lung. So there's something wrong about our attention to PM-10 and 2.5 exclusively. And I think that should somehow be taken into consideration whenever we discuss PM's.

DR. KLEINMAN: It's a good caveat. There are experimental data that show that particles as large as 50 microns are easily inhaled. It depends on which way you're facing in the wind.

DR. SHERWIN: I have molds -- pollens 50 microns.

DR. KLEINMAN: No, I'm just talking about aerodynamic diameter now. So, yeah. The PM-10 is a convenience to some extent.

DR. SHERWIN: Let me also say there are 20 billion particulates on average in every human lung.

DR. KLEINMAN: True. But to be focused on why the standard is focusing more on the smaller size particles, it's primarily that the indications from the epidemiology are that you get tighter associations with health effects and the fine particle fraction than you do with the PM-10 per se -- in many studies, not all, but in many.

DR. SHERWIN: Yes, but if you're excluding things above 10 micra, and they're getting into the lung, you may be greatly understating that adverse effect.

DR. KLEINMAN: Well, I think at the present time, there is no move to exclude the PM-10 standard, even though we're going to focus --

DR. SHERWIN: No, no, but particles above -- I mean, if I'm seeing 35 micra platy particles in the lung --

DR. KLEINMAN: Yeah, but the health effects don't seem to correlate with those at all.

DR. SHERWIN: They always measure.

DR. KLEINMAN: Yeah, well, they have. Well, don't forget, what we used to measure was TSP, which was Total Suspended Particulate, which covered particles from about 40 microns down -- aerodynamic size.

DR. SHERWIN: Well, that data goes way way back and --

DR. KLEINMAN: But that's where they set the first PM standards were based on TSP. Yeah, there were --

DR. SHERWIN: Total suspended --

DR. KLEINMAN: Total Suspended Particulates were the first six studies -- six city studies was based on that. Then they found that they got a better correlation if they looked at just the particles 10 and down, and now, by going down to a smaller cut, we're getting tighter associations. And there are some among us who might say that certain chemical fractions within that fine particle mix might associate better with the health effects than even the total PM-2.5. So it's really a game of what associates better with the epidemiology. And that's what's been forcing our attention.

DR. SHERWIN: Well, let me leave you with the other half which says that the fibrous particulates certainly have had no attention.

DR. KLEINMAN: Oh, yeah.

DR. SHERWIN: They tend to be more noxious than the platy ones.

DR. KLEINMAN: And we haven't got a standard for that in the ambient air. Melanie?

MS. MARTY: Just a comment about the fibers -- two comments. One is that in the work done with asbestos, whether it gets into your lung or not is a lot more dependent on how big around it is, rather than how long it is because it lines itself up with the flow of air, and it just has to be short enough to get around all the bends to get into your lung. And the other issue is in terms of regulating fibers. Asbestos is actually a toxic air contaminant in the State of California. And there are air toxic control measures in place for regulating some sources of asbestos. So we're not ignoring it. It's actually being dealt with in a different program. DR. KLEINMAN: Bart?

DR. OSTRO: I just want to close by saying that tomorrow we're going to switch carbon monoxide and lead schedule to accommodate Dr. Balmes. And did you want to say something about the restaurant?

DR. KLEINMAN: Yes. Let's see, there are six

people who signed up to go to the restaurant this evening. The restaurant's name is Mazzini's. And it's at 2826 Telegraph in Berkeley. And that's about four blocks north of Ashby. And the phone number is 848-5599 for those who get lost. And for those on the committee that are here that need a lift, I've got a car. So we could meet and go over. The reservation is for 6:30. So we probably -- and it's in Bart's name if anybody gets there first. We have a few more minutes. I just had one philosophical note that I just wanted to bring up. When people talk about the standards being set to protect exercising people, in some levels, that's right. But that's sort of taking the direct interpretation view of it. Really when these exercise studies started, it was toxicologists' way of making a two-legged animal model of a sensitive human being. And part of what is missing in a lot of our standards is what we'd call a margin of safety in the occupational setting. Our margin of safety is actually that in order to reset the standard of levels where we've pushed people to very high exertion levels and made the exposure level extreme, where we could not take people who were extremely ill and subject them to this kind of pollution. So we really have to look at in both ways. You can't just take the literal interpretation

of the data. You've got to look at it in the context that what we're trying to protect are the most sensitive people and they're not the people we're going to bring into a laboratory and work with. So that was part of a reason that some of these [inaudible] and dynamic analyses give you very different answers because we're not really looking at that intersection. We're looking at this more as a model than as a real individual sometimes.

DR. SHERWIN: Mike, let me just mention one -- can you consider a PM standard without taking fibrous particulates into consideration?

DR. KLEINMAN: Mike, do you want to --

DR. LIPSETT: Michael Lipsett. I was going to refer this question to ARB staff.

DR. PRASAD: Thanks, Mike. As we consider PM, it's a [inaudible] standard. So I do not think that -- in essence, we exclude the fibers that are. However -- and we say that it's cut off, I do agree that it is an arbitrary line we have drawn over 10 and 2.5. The [inaudible] review has clearly indicated that 2.5 is an arbitrary line and that was only because of the convenience in what the measurements were available. And also, there was clearly a lot of argument about whether one should -- if one is really

looking at this ozone issue, should one be looking at one or below as considerations. So right now it has been based on what observations we've done and what has been repeatedly measured. MR. WESTERDAHL: Dane Westerdahl. Just a little bit more in answer to your question, Russ. The fibers you're talking about are collected and are considered in a standard where an aerodynamic diameter is included. So a very large skinny particle fits within what is collected on that filter. So it is included in this. However, there are other standards, as Melanie mentioned, where specifically take the most harmful identified fibrous materials and go after them. Those are toxic air contaminants, with asbestos specifically. So we have an even more stringent active program to work on those fibers that you're concerned about. If we were just to throw their mass in and say we wanted a PM-10 standard at a certain mass and it was asbestos, it would not be acceptable. If we allowed 30 or 50 micrograms of acute meter asbestos in the air, no one in this room would consider that an acceptable public health protected activity. We go about that very specifically because we know it's very toxic material. So it is considered regulatory activities.

DR. SHERWIN: But it's not measured.

MR. WESTERDAHL: In some conditions it is measured. In ambient air, it is not measured in most places.

DR. SHERWIN: Well, when I was part of the South Coast, I asked if they monitored people. And I said, "Do you pick up the fibers?" And they said, "No. Our monitors are not geared to pick up fibers."

MR. WESTERDAHL: But as mass, they are picking up the fibers, but they are not saying them to make sure that they know on a routine basis how much fibrous material there is. In certain cases, if we have a concern, we do special monitoring to look for fibers and then do the fancy optical and chemical means to determine how much of those fibers we have.

DR. KLEINMAN: Well, I'd like to thank everybody and we'll reconvene tomorrow morning.

(Adjourn 5:00 P.M.)

DR. KLEINMAN: Are there folks here who were not here yesterday? In that case -- there were hand-outs given out yesterday. If anyone did not get one and would like one, if you mark that on your sign-up sheet, Rachel will make sure you do get it. And this morning we are going to begin with the discussion on particulate matter and sulfates. And Bart is going to present the introductory comments on that and then George Thurston will have an opportunity to present his viewpoints.

DR. OSTRO: Welcome back everybody. And once again, we're reminded to speak into the microphone and identify yourselves, and if you cite a reference to try to cite it slowly so that they could get it. So our summary of particles. Basically in California we have two different standards. We have an annual average currently at 30 micrograms per cubic meter PM-10 and 50 micrograms per cubic meter PM-10 for a 24-hour average. And one thing to note relative to U.S. E.P.A. proposed standards for PM-2.5 -- I don't know if everyone can see this -- but what it says is if the ratio of PM-2.5 to PM-10 is .5, then the U.S. E.P.A. PM-10 standard of 15 is roughly equal to the California PM-10 standard of 30, our current standard. So one could make an argument that the standards are roughly similar in terms

of protection But if the ratio is more like .65 which is more likely in most urban areas in California and the rest of the country, then the U.S. PM-2.5 standard of 15, a proposed standard, is more equal to roughly 23 micrograms per cubic meter. So one could argue that the California standard would be less protective than the proposed PM-2.5 standard. So obviously the ratios of 2.5 to 10 matter and how many allowances you allow, whether it's the single highest and so on, and how these things are calculated. But in terms of annual average, the California standard may not be as protective as the proposed 2.5 standard. So regarding the scientific evidence, our review indicated, I think, as most of the people here already know, that there are dozens of studies linking different measures of particles, be it PM-10 or PM-2.5, or sulfates, or COH, linking those different measures as different metrics with a wide range of health outcomes, from very severe outcomes like premature mortality and hospitalization for heart disease or lung disease, emergency room visits, and then more minor outcomes like lung function, respiratory symptoms, asthma exacerbation, and so on. And these things are occuring at current ambient levels with some indication that if you use the means of some of these studies that

they're occuring at levels below the current standards or at the current standards of California -- certainly close to the current standards. Now there's a lot of discussion about who is the sensitive sub-group for those outcomes. And I think the general consensus is that most, but not all -- or much but not all -- of these effects relate to elderly or people with chronic disease. Certainly there have been studies specifically conducted on children asthmatics and children non-asthmatics where we've seen effects. But the more serious effects are thought to be for other than children and infants. But some of these studies, and even going back to the early London studies of the 60's and 70's, indicated that children did have an enhanced risk of mortality relating to higher levels of particles. So children and infants may be part of that group as well. And in addition, there's been several studies now conducted in the last couple years specifically relating to children and infants. Most of these studies are cross-sectional in design, but indicating that children and infants may be suffering from mortality, low birth rate and prematurity in relationship to exposure to particles. These are all from epidemiologic studies, of course. Regarding the concentrations, most Californians are exposed to levels

above the standard. And of course we're not exactly sure which component of PM is the responsible agent. And our recommendation was that in any review of the PM-10 standard, we also incorporate a review of sulfates, nitrates, ultra-fines, fines, coarse, the whole mix in that, and that the sulfate review would be contained within the PM-10 review. So as a result of that evidence, we put PM-10 in the Tier 1.

DR. KLEINMAN: Thank you, Bart. Bart, just as a matter of clarification, in terms of the sub-species, where would you place diesel emissions? Are they considered separately under the toxics program, or are they part of the mix?

DR. OSTRO: Yeah. We do have a toxic air contaminant program which would look at and regulate diesels as a carcinogen. They don't talk much in that program about the non-carcinogenic effects. So whether that rule making and regulatory action is sufficiently protective, probably would have to be examined as well regarding just mass and how diesels contribute to mass. Would you agree with that?

DR. PRASAD: Shankar Prasad here. I mean, in that regard, actually the Air Resources Board recently adopted the Risk Reduction Plan responsible in eight-year period and

there's supposed to be 18 control measures which will be [inaudible] over the course of the next two to four years. And so with that, the projections are from 20/10 with the proposed set of rules. From two days risk levels as in terms of the cancer risk of the nasal, it will be reduced by approximately 70 percent over the next ten years. And for 20/20, that reduction is about 85 percent. And it assumes a couple of things, that the retrofit program that we saw in full swing in the next couple of years, and also the sulfate [inaudible] as proposed by E.P.A. will be interrupted in the next few months, reducing the sulfate content to 15 ppm in the field. And if you look at the diesel contribution as a PM alone, it does not come out in a [inaudible] big source. But on the other hand, if you look at the diesel as a NOX part of it, it comes out as a major piece.

DR. BALMES: John Balmes. However, if there are adjunct effects of diesel, I guess particles in terms of asthma, you know, that's not necessarily being looked at by the Toxic Air Contaminant program, so I think -- I don't disagree with anything you said and it's good news that there are efforts to control diesel exhaust particulate, but I still think that a review of PM should include the evidence for diesel exhaust, particularly as an adjunct for

allergic responses in the airway.

DR. KLEINMAN: Thank you. I'd like to ask George Thurston to come up and give his viewpoints and any additions to what has been said.

DR. THURSTON: Thank you. I guess I just want to start out by saying how appropriate it is and sort of very useful way to look at these pollutants is by looking across the board at children as a group. I think when you look at the E.P.A. criteria documents, they tend to have an exposure section, and in the exposure section they mentioned, well, children are outdoors in the afternoons. And then they have a toxicology section and they mention, well, there are some studies in the toxicology that might relate to children. And then in the epidemiology, there's also mention, but they never really put it together into one place and say how, when we look across the exposure, toxicology, and epidemiology, what does that say collectively about effects. And when I did that, as well as I could with the information that I had and with my knowledge, I think that as you go forward with this, you'll want to get people more involved who are experts more in the exposure part and experts more in the toxicology part to input. But from what I was able to glean from my knowledge and from the

literature was revealing to me, that children really are an especially susceptible group for a variety of reasons that relate to their exposure and to their toxicology, developing immune systems, and also to their behavior patterns. And the epidemiology really reflects that when you stop -- and I started going throughout the old literature and finding with the London Fog episode that less than one year was very elevated -- children age less than one-year-old was a very elevated mortality group in the London Fog episodes. And similarly, Burnett's work in Canada showed that to be a very elevated group. And then the recent studies for infants -- infant mortality, birth weight studies -- also suggest that this group is very susceptible and, well, also implies that perhaps pregnant mothers, since you're looking at birth weights, would be of special interest. I didn't really think that in the review that that really came out as much as I would have liked as an important area for investigation in terms of setting the standard and also, you know, research priorities. I think that we do have a lot more to learn about it. But what we have learned is enlightening and I think important that that sub-group is one that seems to be, based on the evidence that we have so far, much more affected. I think that Bart Ostrow is right, that

historically we looked at this and said, "Oh, this is a problem especially of the elderly." And now we look at this group and we say, you know, people with pre-existing disease are very affected -- well, that's these children. They have lots of pre-existing diseases as we talked about yesterday. And they have developing immune systems, so they've very susceptible. And it could have long term implications to their health if their immune system is affected, as well as the fact that they're more susceptible to effects at that age, let alone later implications. So I guess that's the point that I would want to draw out more than what was brought out in the review. With respect to sulfates, the point about -- the interaction between acid coating on particles is an important one that needs to be looked at. I think Mike Kleinman's work where he looked at carbon particles and with coatings and acid, and their interactions with ozone is starting to get towards that. Most of the research that's been done on acids has been done with pure sulfuric acid droplets. And that's not really the way things are in the real environment. And most of the mechanisms that we look at today would be enhanced by an acid coating, for example, the metals hypothesis that oxidative metals on particles have an effect in the lung.

Well, if you have an acid coating that increases the solubility and the bioavailability of those metals. And it doesn't take much acid. Mike, in your experiments, I mean, if you were to do the sort of traditional measurement that we make of acid aerosols where you looked a micrograms per meter cube of acid on those particles, I would assume it would be very very low because you're just coating the particles rather than having a pure acid droplet, right?

DR. KLEINMAN: The mass of the sulfate on the particles was about 50 percent of the total mass. So it wasn't as thin a coating as you might get from just deposition from --

DR. THURSTON: So what would that be in terms of micrograms per meter cube?

DR. KLEINMAN: I believe for our experiments, we were operating at about a total of 200 micrograms per cubic meter of total particle mass. Half of it was sulfate, half of it was --

DR. THURSTON: Oh, well, so that's more substantial than I would have guessed based on what I've seen. But I know that L.C. Chen has done some experiments where he took pure sulfuric acid droplets and then he took particles coated with very small amounts and he got exactly

the same response for those two where one had lots of acid and the other had very little. So also that's carbon particles which I wouldn't think would be very activated by acid as much as a real particle, sort of a typical particle, let me say, that we have out in the atmosphere that would perhaps have metals from a combustion source, although certainly carbon does result from combustion as well. So anyway, I think that those results sort of do get at a first step towards looking into this issue of acids, the way we measure them and the way that we evaluate them, that needs to be looked at more, and especially with respect to the sulfate standard, that certainly the state of the sulfate makes a difference. So we may want to consider that in setting the standard for sulfates, a place where you know that the sulfates are neutralized would certainly be expected to have less of a health impact and than a place where the sulfates are fresher and therefore more acidic. So that's an aspect that's difficult to address because there isn't very much evidence and very much data available, let's say, to look at this. The data that are available would indicate that more acidic sulfates have more effects than less acidic sulfates, and especially when they're coated on particles. So I think those are aspects of the

sulfate standard that you may want to try and look at when it's been reevaluated.

DR. KLEINMAN: Thank you very much, George. I'd like to open it up now to comments from the committee and consultants.

DR. PINKERTON: Kent Pinkerton. I'd like to just make a comment on the review. I thought it was extremely well done, George, and also to emphasize the importance of how children are very different from adults from the perspective of they don't have a fully mature immune system, they also don't have the ability to metabolize many of things that are found in our environment. And all of those factors, I think, play a role in the type of sensitivity that I think we're beginning to see in the epidemiology based on looking at children's responses to particulates. And I think that that really emphasizes the importance of really taking a careful look at the current standards to make sure they really do adequately protect children.

DR. OSTRO: Kent I wanted to ask you -- this is Bart Ostro -- yesterday, Ira Tager made the statement about ozone controlling for baseline health conditions, he wouldn't expect differences in adults vs. children. Do you want to say, or anybody else, what your feeling is about

exposure to particles, again controlling for baseline status, whether there might be differential effects for children vs. adults.

DR. BALMES: I don't think Ira said that he wouldn't expect differences, that there wasn't evidence for difference of different ones.

DR. PINKERTON: And I think if you're saying, Bart, that you would control for ventilatory rates, deposition, and just simply say are these particles more of an adverse effect in children than they are in adults, my feeling would be that there tremendous potential for that occurring based on the fact that children do metabolize things in a completely different manner. We've been doing studies recently in looking at combustion products basically in a system where we can generate soot and then add in transition metals into the soot itself. And we've been doing these studies in rats in looking at the effects in adult rats vs. neonatal rats. And we see similar responses in both ages of animals. However, the magnitude of the response in the young animals is much greater than it is in the adult animals. Again, we don't have enough data gathered yet to say that there's a statistically significant different between neonates and adult animals in these

studies, but just looking at the data itself, you can see that the magnitude of changes is much higher in these young animals compared to the adults.

DR. THURSTON: Bart, I might comment on that. I think if you look at Table 6, page 17 of the section that I wrote, you know, there's a couple of points that can be made from that. One is that the excess risk, the percent increase, was the highest for children less than one year of age. But even if they had the same percent change for the relative risk, as we saw yesterday, the underlying rates of these diseases, the incidence is much higher for less than one. You have to be careful, I think, when we look at these when we're trying to compare age groups, not just to look at relative risks. You have to also look at attributable risks. And I make that point in the write-up because, here, for lets say asthma admissions, you're talking about double the percent increase in respiratory hospital admissions for asthma for children less than one vs. people 75 years of age or older. But we saw yesterday that the rates were double, triple, underlying. So that percentage is times a bigger number. So when you're looking per 100,000 individuals, you're going to get a much bigger number for the less than one year of age. Even if you got the same relative risk.

And this also carries over to when you look at minorities that they have higher underlying risks. So I've seen published in papers -- Joel Schwartz had a paper not long ago and he said, "Well, I don't see any difference in the relative risk for..." and I believe it was hospital admissions for blacks vs. whites, but what that fails to address is the fact that the hospitalization rate was much higher for blacks to begin with, such that the impact per microgram per 100,000 people was much higher for minorities given the same relative risks. So I think you have to also consider that when you're looking at different age groups. Comparing relative risks is dangerous if you have different populations that you're comparing.

DR. PINKERTON: Kent Pinkerton. I also wanted to make one other point too. We often times think about children and injury to those children and whether we've got an inflammatory response compared to adults. I think it's very important to keep in mind also that injury has to be followed by repair. And the repair process and the repair mechanisms in children are very different than they are in adults. Certainly from an experimental perspective, we found that many different types of toxicants that can be inhaled into the lungs that produce an injury, especially to

specific target cells lining the airways of the lungs, an adult animal will develop a tolerance to that and they'll actually develop a point where they actually no longer respond to that injury. And they repair in such a way that they replace injured epithelial cells with absolutely the same type of cells that are completely normal. In contrast, if those exposures are done in a neonatal animal, we find that often times the injury occurs as it does in the adults, but the repair process leads to a completely different anatomy of the lung. Rather than having cuboidal epithelium with ciliated cells, often times you can actually find that you develop squamated epithelium that does not repair in a normal fashion and can persist for a long time. In our studies so far, this is based on months. We don't really know what happens after a longer period of time for that, but it's another consideration to put on the table.

DR. THURSTON: George Thurston again. Do you have a reference for that yet, or is that ongoing work?

DR. PINKERTON: That's work that actually you might have quoted some of it -- it's Suzette Smiley Jewel. It was one of your references where she talks about the inability for repair to occur in neonates compared to adults.

DR. THURSTON: Right, yeah, that was in the section. Yeah, that's a point that Ploper and Panouchi make in their recent article and reference that work. That's a good point.

DR. PRASAD: Kent, is that applicable to PM specifically, or is it not applicable to any pollutant in an [inaudible] animal, irrespective of whether it was an ozone damage or a PM damage, or any toxin?

DR. PINKERTON: That particular pollutant that they were looking at was nitronatholene. And actually that can be found within cigarette smoke and I don't know if it's actually a combustion product or not, but I think there can be some parallels made between that and PM. But again, that was a very specific set of toxican that they were looking at and an inability of the lungs to repair. But we've also done studies with environmental tobacco smoke and we've often wondered, well, is environmental tobacco smoke behaving in a similar manner that PM does. Again, we have done studies where we have done very low concentration exposures to environmental tobacco smoke and have found that neonatal animals respond in a very different manner than to adult animals. In fact, neonatal animals will actually develop a hyper-reactive airway or a ticklish airway that we

never see with similar exposures in adult animals. And again, the question that we have in our mind now is would PM perhaps mimic that same condition, but we don't have an answer for that.

DR. PRASAD: So you think that the PM damage could be higher than gasses, any kind of [inaudible] damage?

DR. PINKERTON: That I would say -- I don't know how to make those comparisons -- but certainly when it comes to gaseous pollutants, I think we see more of a clear anatomical change that takes place both in neonates and adults.

DR. PRASAD: To the same degree?

DR. PINKERTON: To the same degree? Well, within the same locations. They tend to be areas that are in the transition from the conducting airways to the gaseous exchange region, so it's within the centri aspir regions. We also see that it tends to be along branch points along the bronchial tree.

DR. BALMES: Just a note. So your environmental tobacco smoke studies involve exposure to both particulate and the gaseous phases, right?

DR. PINKERTON: That's correct.

DR. BALMES: So I think it's a good model for the

pollutant mix perhaps, rather than PM alone. That would be my comment.

DR. SHERWIN: Gleason published a paper a while back in which he talked about childhood respiratory trouble and Bourroughs also mentioned that children who had some type of respiratory disease were more likely to be the ones who developed chronic lung disease later on. To use the concept of childhood respiratory trouble says that we don't really know what's going on. But the point is they become a very susceptible group when you talk about air pollution. So the question I have is do you -- I wish Mark Frampton were here, as well as Ira, to help with this question. Maybe John can enlighten us as to what the latest feeling is about a susceptible group of children who have what we call childhood respiratory trouble.

DR. BALMES: Well, I think you're correct that epidemiologically it's well established that kids with lower lung function, for example, when you test them tend to have worse outcomes long term in terms of lung function and respiratory health in general. Whether we understand the basis for that or not is another story, and I don't think we do. So I don't know how much more we've advanced over the basic concept of respiratory trouble for kids. But your

point is well taken. Kids who get into respiratory difficulty are more likely to have problems later on in life in terms of respiratory health.

DR. SHERWIN: Would that not then mean that one of the sub-straits we should be seriously considering in any kind of particulate or any other pollutant testing is this sub-set of the population of children with childhood respiratory trouble?

DR. BALMES: Well, I think that was one of George's points, actually, somewhat analogous to the adults with preexisting disease. I thought he was making the point that many kids have coexistent disease.

DR. SHERWIN: Well, we sort of think about immunologic disease or there's a whole group of them, but in line with what George Thurston was saying, it would be nice to put all these things together. One group for sure which we don't know much about but is identifiable apparently is childhood respiratory trouble. So my point is maybe that's a great subset to study.

DR. BALMES: Yeah. I don't know how easy it is to define childhood respiratory trouble, but kids can be defined in terms of their risk for asthma. That work is actually fairly far advanced, so that kids who have wheezy

bronchitis that will wheeze with colds are more likely than kids who don't wheeze with colds develop asthma later on, even controlling for other factors. But the concept of childhood respiratory trouble is bigger than just asthma.

DR. SHERWIN: Yes, that's the point. I'm sort of taking the Thurston principle, which says there's immunologic things over here, there's asthmatic over there, but maybe they all come together under what would be called childhood respiratory trouble. You'd have a nice big group to study.

DR. THURSTON: Well, and I think especially the infants. Less than one is -- I'm telling everybody that I run into who has data sets, okay, because generally when we looked at epidemiology, people look at 14 and under, or they might break it out to five and under, but not many do. So I'm saying try just aggregating your data more. Try looking at that infant population when you do your epidemiology. I hope that people will start doing that more. What limited evidence we have so far would suggest that's a very effected, very interesting group to look at, as you say.

DR. WHITE: This is Mary White. You know, I'm struck by the discrepancy between current exposures and the current standard. And it seems that if you could get better

compliance or fewer exceedances of the current standard, there would be public benefits to that. Is the thinking that if you reviewed the standard that you'd develop some insights that may simulate a more creative or more innovative look at current efforts to reduce exposures that might ultimately result in better improvement in terms of air quality now?

DR. OSTRO: Well, there's a couple issues there. One is that we haven't reviewed the standard for 17 years and I think just to get up to the science and have other stakeholders be aware of what the science is is important. A second issue is whether the PM-10 standard by itself should be sufficient, or whether we should look at subcomponents, possibly including separate PM-2.5, or of course particle standards, or ultra fines, or whatever the best science will tell us. So I think those are the major issues relating to the potential for a review.

DR. PRASAD: Those are the second ratios compared to the SB25 focus, right? I mean, in terms of the SB25 focus, the priority is dependent upon the children's susceptibility to one vs. the other? I mean, the issue of your inclusion of the coarse, fine sulfates, ultrafine, will happen whenever this review -- I mean for the PM review?

DR. OSTRO: Right. I mean SB25 targeted children for sure, but it also said protecting other susceptible groups as well. So even if children were not particularly sensitive, but other groups were, that might give us reason for a review.

DR. KLEINMAN: One other issue that hasn't been approach, going back to the time, you know, the averaging time that's being considered. We look at 24-hour and annual average data because that's what's being measured. But the animal toxicology work is often done with very short term exposures in that scale, and often has shown damage to lungs and tissues. There might be some advantage to considering short term exposure to PM as another basis of a standard. And I think that might be part of the process as well.

DR. THURSTON: I agree with you, it's an interesting thing to look at. But to this date, for the epidemiology, if you want to have supportive evidence from epidemiology, you're going to have trouble finding it because in the epidemiology, we largely look under the lamp post, we have to use what's available, and so what's available are 24-hour averages. So then you set the standard based on what you know. And so I think as perhaps we get into putting more of these Tions, for example, where

you get hour by hour particle mass measurements, that you might start to be able to get some epidemiology that would look at that. I know Ralph Delfino has a paper he published in the last couple of years looking at young people and -- was it lung function -- I think it was lung function -- and symptoms -- in asthma, was it? Yeah. And I remember the key thing was he had looked at an eight-hour average and found stronger associations with an eight-hour average than 24. But that's about the only paper I can think of where somebody had that kind of data to look at. So that's the quandary you have in setting the standard for less than 24 hours. I go back to when we set the PM-10 standard, and I think a lot of us who were doing the research felt that a PM-2.5 standard was appropriate back then. But E.P.A. didn't have any PM-2.5 studies to base a standard on, so they couldn't set it. So they went to the PM-10 where they had the studies. And then as more and more PM-2.5 data became available, they were able to set a PM-2.5 standard which I think many people thought was probably the appropriate thing to do in 1987. And I think the same may go for these less than 24-hour concentrations.

DR. OSTRO: Regarding shorter term averaging, my colleague Dr. Lipsett here put together a workshop a couple

months ago to look at high exposures, short term exposures, maybe one-hour exposures to fires and other combustion processes. And we did a review of literature and we saw your paper, of course, Mike, as well. One of the things we found is there's certainly not a lot out there. The Delfino paper is somewhat equivocal if you look at it. Sometimes he finds 24-hour averages are better, sometimes shorter term averages are better. There are a couple other studies now showing short term effects of two-hour averages -- Arden Pope's paper showing heart rate changes in two hours in response to ETS exposure. And there's another heart rate study out showing four-hour averaging shows effects. And besides the Tion, there's a lot of people now that are using beta gage. We have several studies where you have one-hour averages from beta gage monitors. So I think more people will be able to look at that type of information. And perhaps when we do get to reviewing particles whenever we do it, maybe there will be a little more information out at that time which will help in terms of averaging time, both for standard setting as well as for warning systems and so on when we talk about fires and other emergencies.

DR. KLEINMAN: Great. We have a little more time and are there any more comments from the committee or

consultants? We can take a few brief comments from other participants then. Jaro, okay.

DR. VOSTAL: It is just only a question. If you remember when we were discussing yesterday the probablistic aspects of the exposure. When you, George, are talking about the neonates and you are talking about the one-year-old, how much of the outdoor exposure do they get so that you can correlate it with the stationary monitor outside? When you are discussing the PM-2.5, obviously, it has been discussed in a very extensive way that the concentrations are penetrating much better into the indoor houses, but certainly not for the PM-10. And the same applies also -- you know, when we are talking about the role of the neonates, there's probably very correct whatever you can see, but how can we apply it that it will be reflecting the outdoor exposure?

DR. THURSTON: Well, I think a key thing to remember is that when we're setting a standard, we're talking about exposure to particles of outdoor origins. And the recent literature, if you look at the paper that just came out by Mage and Wilson and others -- I think it was in the Journal of Air and Waste Management Association -- came out and made the point that when you're doing an

epidemiologic study where you've got many people involved, the personal exposures and the indoor exposures to particles of outdoor origin correlate well with central cite concentrations. It doesn't take long for these particles to permeate indoors. And that is the source air for indoors as from the outdoors. So I think that it's less of a complication, and certainly for PM-2.5, as you point out, Jaro, that that permeates readily. So I don't think it's as big a problem as we used to think it was. DR. VOSTAL: If we are talking about this situation about 2.5 or even PM-10, we have to realize that even indoors are completely different sources of the exposure. In the same issue, if you are quoting about the [inaudible], you can find also a new paper which is coming out by Christopher Longklund who is from [inaudible] Group. And I think the paper is extremely informative since it is showing that with every single activity, whatever you have at home, walking vigorously and particularly, for example, frying an egg, burning bagel, baking, and so on, you are having unbelievable changes in the exposure for the people who are inside. So if we are so much concerned about the low concentrations which we can measure on the outdoor exposure, now what does it mean? That we are seeing that people and

particularly those neonates and the children before they are walking, they are always staying only inside and that they might be exposed to completely different sources of pollution.

DR. LIPSETT: I wanted to ask the ARB then, in terms of control strategies, would you be trying to impose some sort of manufacturing requirements so you have low emitting bagels?

DR. VOSTAL: I suppose he can see what he can find out. But before we come to the conclusions of the epidemiology studies which are taking the stationary monitor and correlating it with the mortality of the neonates, then obviously they might have really some programs.

DR. KLEINMAN: Jaro, one consideration in this though is when you look at the cross-sectional studies and you look at cities that have more pollution vs. cities that have less pollution, there's no reason to believe that the level of cooking, frying bagels, making eggs in those cities is going to be greatly different, so that the epidemiology may be not as sensitive as it might be if there were none of these indoor sources. But it's still picking up an influence that associates with the outdoor source. So despite the fact that there are these other competitions,

and despite the fact that we tend to spend an awful lot of time indoors, the fact remains that the association between these health effects and outdoor pollution is measured mainly by central monitoring sites, has an association.

DR. VOSTAL: I think you are absolutely right, but you have to differentiate that what you are talking about is the long term potential consequences of the exposures and so on. But as you really know, the concerns about the PM-2.5 started from time series studies which were comparing day by day pollution with the daily mortality and so on. And so this is really then only for one single city. And also there is a consistency. You can find it from one city to the other city as well. But, you know, we don't have any comparison that all the people are exposed exactly to the same indoors environment.

DR. THURSTON: Yes. And it's not necessary that they be. The thing what you're looking at is the shared variance that they all have. I think if you look at the Mage [phonetic] paper again, you'll see this to be the case that, yes, any one individual is going to be higher than another, and another lower, but when you average over all the people, they tend to go up and down. They have the same underlying driving force in their exposures upon which their

personal additional things are superimposed. And I think that what this says -- I'm not saying that indoor sources are without adverse health effects, it's just that those aren't the ones that are being ascribed to the outdoor pollution. The outdoor pollution is monitoring the particles of outdoor origin, and that is associated with adverse health effects. The variations around that on an individual basis may also be associated. And that's a separate area. Are you on behalf of GM recommending that ARB start regulating inside people's homes?

DR. VOSTAL: I would like to say that I am really a private citizen. I don't want to talk on behalf of anyone, only on behalf of me. And when it comes to the point of how should we do it, then without any question, should we have something that is called "personal exposure." And although Verson and Make [phonetic] are trying to approach it with statistical metal erosion and so on, it is really something that would be much more important if we can only measure to what the people are really exposed. And as you know, we are using epidemiology studies as proof of the causality. And we are having so many factors which we are not aware. We are not controlling for and so on. And so it's very difficult. The statistical associations are

absolutely correct, but are they really the factor which is responsible of it, or are they just only an incidental association between those two elements? Maybe you can answer it.

DR. SHERWIN: Let me mix a little lightness with some science. I have a son who has carried on his mother's tradition of nobody goes into the house with shoes. They're either covered, or you take off the shoes, or you wear something. And I always had raised eyebrows until I read the P-Team study showing that the particulate content indoors was 50 percent higher -- we're using personal monitors -- than outdoors. And everybody knows this know, is that personal cloud of dust that everybody walks in. So I'm very impressed by the fact that indoor particulate is perhaps just as hazardous, if not more, than outdoors.

DR. KLEINMAN: But I think the question is how much of that indoor particulate is of an outdoor origin, because we do have both contributing, especially if taking off your shoes prevents you from bringing in some of the things that actually become part of the airborne --

DR. SHERWIN: I raised that to say that I think that there is sort of pressure on -- obviously, you bring in a lot of outdoor particulates, aside from what blows in

through the windows.

DR. OSTRO: I'd like to get back to the question of infant susceptibility or children's susceptibility. And earlier, John Balmes mentioned children with lower lung function might ultimately be more susceptible as adults or have additional respiratory problems as adults. I want to ask about acute conditions and maybe again to Kent or to you, Mike, what about children or infants with respiratory infections? Can you just talk a little bit about how much more susceptible they might be to particle exposures of different types during a respiratory infection?

DR. PINKERTON: I don't have any information from my own personal experiences in doing studies like that, but certainly we do know that with increased infections that there are lots of things that would lead to potential problems with dealing with particulates -- with inflammation and things like that. But one experience that we're going through right now is actually looking at what happens if there are conditions that exist such as allergen exposures during neonatal development. And we've been looking at this from the perspective of looking at house dust mite allergen as something to sensitize an infant monkey, and then looking at the subsequent effects of exposure to different types of

pollutants. And one of the things that we have noted is that any exposure to an allergen -- and maybe this may also be true for other types of bacterial or viral conditions -- lead to a complete remodeling of the lung. We actually can lose airway generations through the formation of alveolar outpocketings along the airways in an abnormal form. We also can find that in that transition zone between the conducting airway and the gas exchange region, that we can actually develop smooth muscle hypertrophy. And we found under these conditions that these infant monkeys actually become extremely more sensitive to the effects of ozone. We haven't really done any work with the particulate matter. But I think there is evidence to suggest that there certainly could be tremendous effects that could take place. But again, unfortunately, I don't really have any experimental data.

DR. KLEINMAN: The only experimental data we have was from something that inadvertently occurred. We had one experiment where we found out after the exposures that there was infection in some of the animals. And in that particular study, we found that the response to a particulate exposure was very exaggerated -- much higher than we'd ever seen. We thought we had hit something really

phenomenal until we went back and decided there was an underlying infection. There was still a big difference between the controls in the exposed group, but we couldn't use the data. But I do believe from looking at that and looking at some of the other things in the literature that just an underlying infection will raise the sensitivity to pollutant exposures. And that would probably include ozone and PM.

DR. PINKERTON: Again, along those same lines, we had a similar unfortunate experience that Mike is referring to in which we were working with young adult rats. And in those particular studies, we were actually using soot with iron oxide particles. And in that particular study was where we saw that there was a significant increase in the inflammatory index within the lungs of the animals that were exposed to the soot iron matrix. But we also some inflammation in the controls. But it was statistically different, significant, the differences between the two, but we couldn't use controls that had an infection. So there is some correlation even in the animal studies.

DR. LIPSETT: Did either of you try to publish these data because, I mean, I think it would be useful to have, but there's a lot in the literature on the infectivity

model used for NO2 and for ozone, and to my knowledge, and you can correct me if I'm wrong about this, this has not been something that's really been examined systematically at all looking at particles. And I think it would be useful to have that out there to be able to provide at least some tox data that would bear on the question that Bart raised, and that is, for humans who have some sort of infection, does that render them much more susceptible to the effects of particles.

DR. PINKERTON: There actually may be some things out in the literature from Judy Zellkoff on this issue, but I don't know if she looked specifically at young animals. But she was looking at the degree of infectivity and how particulate exposure actually enhanced the degree of infectivity in the lungs of rats, I believe it was.

DR. LIPSETT: I know it's wood smoke that she was using.

DR. PINKERTON: Was she? Okay.

DR. KLEINMAN: Now we've never tried to publish that data because without an adequate control group, it's very hard to make any real conclusions. But I agree with you, it might be an interesting thing to try to accumulate that sort of information throughout the toxicology

community. It might be worth -- here's where the internet might be a useful ploy to try some time just to ask people to provide that kind of information and whether they've had these kind of experiences before. I think we'll need to cut off the discussion now on PM and move to sulfate, which I believe -- the sulfate was pretty much incorporated. George, did you want to say anything more specific --

DR. THURSTON: I think I made my comments with respect to sulfates and the major points on that.

DR. SHERWIN: Michael, I do have one comment in reference to that question about respiratory infection. There is a report, the source of which doesn't immediately come to mind, but the title had something like, "Bronchiolitis, a Poorly Recognized Danger." It had to do with children. They die unexpectedly, especially with minor procedures. And I have had this experience with the Department of Coroner where we get some young child or a 16-17-year-old having a dental extraction or something like that, and they suddenly die. And they have an autopsy of pretty severe bronchiolitis. It shows a sub-clinical type of disease. So what I wanted to point out is that a lot of respiratory infection can be very serious and yet not be clinically appreciated, and it can do what we call putting

the person -- skating on thin ice -- the principle is skating on thin ice. It cuts out your lung reserve. And when you get exposed to something like this, you simply break through. So one should not underestimate the croupy child with or without manifestations that are severe. They can have bronchiolitis. And remember that old principle that 15 percent of your lung with respiratory bronchiolitis is 100 percent impact on air flow.

DR. THURSTON: To follow-up on that point, I think that you can learn something by analogy with the elderly and that recent paper by Zanobetti and Schwartz looking in the elderly where they have data and looking at a group that had prior or concomitant respiratory problems, they found a much higher relative risk from pollution -- I believe particulate matter exposure -- in terms of hospital admissions than those who did not. So that suggests that having -- and there's been other evidence in the elderly previously that having a previously existing respiratory problem will increase your susceptibility to PM. You know, one thing that I thought I would mention that I didn't mention about sulfates was really sort of a -- the recent evidence looking -- that Samatz Group did for HEI finding much higher relative risks for PM in the Northeast, combined with some

recent papers that have found sort of equal effects for coarse particles and fine particles out in places like Arizona, there's a suggestion there to me that in the Northeast where you have higher sulfate levels, that there may be some activation of the particles, whereas otherwise you would have fairly similar toxicities between let's say -- and this is a hypothesis based on a very limited number of studies right now -- but you might have more similar health effects from fine and coarse PM-10 when you add in sulfates. It enhances the toxicity. Now that fits in with some of the studies that have been done down at E.P.A. -- I can't give you a reference off the top of my head -- where they looked at the metals and then found that when, you know, from ROFA, Residual Oil Fly Ash, that the acidic water soluble and higher in sulfates component was the one that seemed to have the greatest impact for certain outcomes that they were looking at. So, you know, I think that in looking at the sulfate and the PM, it may be that particles with -- and again, I'm going back to the acid coating -- this is sort of an observation that I'm noticing as I look through the results of this new study that looked at 90 cities in the United States -- San-Woodall for HEI. I'm wondering why the relative risk seems to be higher for the Northeast vs.

the rest of the country.

DR. OSTRO: Yeah, this is Bart Ostro. The other region that was high though, of course, was Southern California or the West in general, where you don't have as much acid. So you need another hypothesis for that --

DR. THURSTON: Well my recollection was that the Northeast was higher than all the rest.

DR. OSTRO: Yeah, but I think that's the case, but the Northeast and -- I don't remember how California was included, whether it was California alone or the Southwest, or whatever, but it was certainly the second highest -- those were the two highest by far.

DR. THURSTON: Well after the Northeast I would think, you know, historically and even today there's a fair amount of sulfate around California. It's not inconsequential, you know, annual averages of what? Five micrograms? I don't know. I think the numbers we have here are like maximums. It's hard to get an annual average out of that. So California alone wouldn't sort of go against that, but I thought the Northeast stood out much more so than anywhere else. I don't know, it's something to look into anyway as you go through the data, if you're looking at this PM and sulfates standard. It's certainly not -- it's

just a thought that I had in looking at the literature since I did this review as a possible hypothesis that would fit in sort of with some of the past evidence.

DR. OSTRO: Well, I think a related issue then is whether we should in fact fold a sulfate standard into a PM-10 standard in California, or whether that would not be controlling enough and whether we would need a separate standard for sulfate or related species. And our sense of it was that we could fold it in.

DR. LIPSETT: This is Michael Lipsett. George, I think that was a question to you.

DR. THURSTON: It didn't sound like one. It sounded like a statement. Yeah, I think that would be something that you should look at when you're setting the standard as to how to formulate it -- whether days with higher sulfate along with the particles -- and it might be a way to separate out the more rural California particle problems from the urban particle problems, and so maybe that would help discriminate a little bit. You know, we know that all particles are not the same. PM is really a pollutant class, not a specific pollutant, which is why it's so challenging to study in the environment, in epidemiology, and also in toxicology because it depends which particles

you use to some extent. So I think that it is appropriate and I think it's been brought up before that we do in the future have to start considering not just the mass and size, but also the composition. And I think California has gone ahead of the federal government in setting a sulfate standard, which I think is a start. And of course we have the lead standard. But we need to do more of that kind of thinking.

DR. KLEINMAN: I think the question is whether there's sufficient data to substantially say that the sulfate standard provides more protection than the PM-2.5 standard might. And I think that would be an important consideration in deciding whether to fold it in or not. I think George made a good point though that it does differentiate at least between some of the rural emissions vs. the urban emissions, although a major fraction of the sulfate at least in California is not from direct emission, but from secondary production from SO2. So transport would be very important in that respect.

DR. THURSTON: Right. And that would tend to be acidic -- the SO2 formation. But I thought also there's a problem with sulfates from the salt beds. Is that right? I remember seeing some of the data. If they eliminated out --

where was that? It wasn't my section, but -- when they were looking at the sulfates -- I don't want to get into this if you don't --

DR. KLEINMAN: You're looking at the data on China Lake?

DR. THURSTON: Yeah, China Lake.

DR. KLEINMAN: On B-18, there's a graph.

DR. THURSTON: B-18 -- yeah, what was the story with that? And I think they mention the dry salt beds as a source of sulfates. You know, I think it's pretty obvious that that's a very neutralized sulfate. And there's a reason to start thinking about acid sulfates because you do apparently -- is there anybody from ARB that wants to talk about this question of when you eliminate China Lake and then it changes the trends, and you lose that huge peak -- what was going on in that year?

MR. WESTERDAHL: Dane Westerdahl from the ARB. Let me try to give you a little more information about sulfates in California. The dry lake beds are areas of inland lakes that dry up -- are mostly dry at this point. And during high wind conditions -- they're also areas that don't have much population around them, and that's neither here nor there, but they're back behind the Sierras. When

high winds occur, the dust contains lots of salts, blows through the region and has exceptionally high values of PM any way you express it. And there are sulfates in that. And it is in fact a neutral sulfate salt. The other sulfates in ambient air in California, at least from what I recall from our monitoring where we would look at the acidity and the nature of the sulfates using like George Allen's sulfur analyzer is that we almost never had free acidity sulfuric acid, a sulfate. Our sulfates in our atmosphere are either wholly neutralized or partially neutralized. So we don't have much in the way of free acidity in our California sulfates.

DR. THURSTON: Are you using the thermal ramp technique?

MR. WESTERDAHL: Yeah, so that's --

DR. THURSTON: Well, that's true in the Northeast as well. We don't see much sulfuric acid, but what we see is --

MR. WESTERDAHL: Ammonium sulfate and ammonia bisulfate.

DR. THURSTON: Ammonia bisulfate, which is a strong acid.

MR. WESTERDAHL: Right.

DR. THURSTON: Yeah, that's the bulk of the acids that you see because sulfuric acid, the first hydrogen ion is very labile and reacts quickly. The second one is less so, so that's primarily the form. And that's the quandary with that Roger Tanner technique that George sort of perfected, was that it only gives you the sulfuric acid, a part of the acidic sulfates.

MR. WESTERDAHL: As a clear marker. And it combines ammonium sulfate and ammonium bisulfate, as I recall, as one specific number. But in general, our sulfates are not highly acidic. They are mostly neutralized.

DR. THURSTON: Yeah, well certainly the dry lake bed thing which -- so that's another complication with the sulfate standard that has to be considered, I think, in setting the standard, you know, which tends to lead me towards thinking about trying to set an acid standard and then collect acid data and then see -- I mean, one of the problems we've had with evaluate this whole acid hypothesis is that it's not regulated, so therefore there are no data for it. So therefore you can't evaluate it very well.

MR. WESTERDAHL: On a state-wide basis, we had a program called our Acid Deposition Program where we did

monitor both wet and dry deposition in at one time probably about two dozen sites, everything from very rural pristine environments to highly polluted environments. And again, we were not finding high levels of acidity in either our wet or dry deposition. When we did find acidity, it was from nitric acid, not sulfuric acid, which is another question about acidity. But it's not going to be -- it's not PM, it's acidity.

DR. THURSTON: Right. Well that does bring up the nitric acid question which really hasn't fit into the scope of what we're doing here in the last couple days, but does sort of pop out when you look at the Peters study, Children's Health Study. And I did mention briefly in my section just as a possible interaction there between nitric acid which should be scrubbed out by the nose and throat, and yet they're finding associations -- you know, it's one study -- but that's another issue that needs to be looked at in the acidity question that maybe that's riding particles into the lung and having adverse effects -- again, interaction with particle and acid in that case, perhaps.

DR. KLEINMAN: I think another important aspect with the sulfate question would be particle size because things like the China Lake sulfates are probably going to be

in the coarse particle mode, greater than 4 microns because they're resuspended from deposited material, whereas the material formed in the atmosphere is much more likely to be below one micron in size. And deposition would be quite different.

DR. THURSTON: I don't know how they were originally in 1984, whether they were using TSP perhaps? Or PM-10? How long have they had a PM-10 standard again -- here in California? '85, so maybe these were TSP samples that were analyzed for sulfates in China Lake? I don't know. So perhaps using the PM-10, it would eliminate that problem, or going to the PM-2.5 measurement technique, as you say, you'd be able to separate out those very alkaline sulfates. But I guess we digress.

DR. KLEINMAN: Are there any other comments?

DR. LIPSETT: This is Michael Lipsett. A lot of this discussion has been very interesting, but in a way it doesn't really bear directly on the kind of issues that we have to decide in this whole SB25 process, which is which of the different pollutants we need to put at the top of the list for possible review and revision. And I guess I just wanted to get a sense maybe from George and possibly the other individuals here as to how they would look at the

effects of PM on children and other susceptible subgroups in relation to the other pollutants we've examined so far in terms of I guess the overall impact on public health.

DR. KLEINMAN: Well I think that's an interesting question to raise and we do have time to address it. We've really covered what I would think of as the major contenders for Tier 1 and so we've already discussed PM, sulfates, ozone, NO2, SO2. And it might be good to try to get a sense of how we think of these things in terms of which of these things we would take first. You know, which would be the highest priority? I really don't believe that we'll get a whole lot of serious contention that lead or CO are going to be the first thing we have to attack. Kent?

DR. PINKERTON: This is not in response exactly to your question, but I did want to ask George or others here about Table 9 in your review where you talk about the sensitivity in infants and health effects to long-term PM exposure. We've been talking about acute exposures. But the question I have in my mind is that during pregnancy and the unborn child, is there a clear PM effect? You've listed a number of references that seem to suggest that, but how strong of an association is there with PM exposures and effects on the unborn child? Or are those effects something

that are manifested after the birth of the child such as conditions of infant mortality, SDS, etc. It's on page 23. And again, many of these are coming from Eastern European countries from the Czech Republic.

DR. THURSTON: Right. I think you raise a good question. I don't think we really know the answer to that totally. But if you look at birth weight, that would imply effects before birth that in utero and effects on the mother. The Shea & Greenstone study, which is not yet published I think, it's probably in press -- I think they're at U.C. Berkeley, aren't they? You're nodding yes. And that study is one I think that should be encouraged to get into publication. When I last checked with them, they said they were going to submit it this Fall. So it may be submitted for publication. But that's a study that's been done inside the United States. And then Ritz and Yu -- although most of the studies are done outside the United States. There are some in confirmatory studies. And then, you know, Woodruff -- but of course, Woodruff only looked at particles. So I think a lot of these studies may not have looked at the full suite of pollutants in order to eliminate them. I thought that Bobak and Leon's follow-up study -- and it isn't much more an elegant study than the first one

then did or than Woodruff's -- where they had matching and also they looked at multiple pollutants, so that seemed to focus on the particles more so. But certainly there's a need for more research on this to further clarify the questions that you raised. But certainly I was really -- I've never really sat down and gone through this literature myself and I was taken aback by the consistency and the effects that were documented for infants. And then when I started looking at the toxicology, I found biological plausibility for these effects. So I really think that this is an important topic to consider in setting regulations as well as in future research.

DR. SHERWIN: George, do we have any data on relative proportion of those who are admitted to emergency for respiratory trouble, those who are seen by physicians and don't get admitted, and then those who never come to attention? Has anybody tried to find out what the pyramid looks like?

DR. THURSTON: Yes. There's some evidence -- available information. Of course, I'm sure that varies from place to place depending on health care practices. There was some work done in New York that said about 12 percent of children going to the ER for asthma problems were admitted.

So that would mean, you know, you're talking about something like eight times as many people coming to the ER visit as admitted. And then doctors' visits -- there are some studies that have been done in England -- Hajat -- and also in France -- a Medina, I think. And they found many times the numbers of hospital admissions, people went to see their physician. And even more so than the hospital visits. But I can't remember the multiplier factor. But yeah, this has been looked at. And it is a pyramid. So when we do look at mortality and hospital admissions, we're really only looking at the peak of the effects, and there's a much broader range of people who are affected that are never accounted for by usual statistics. Usually doctors' visits are not recorded centrally. And I think we do have an opportunity with the new databases, if you go here in California, the HMO's have that data that can be obtained and analyzed. And I think that's beginning to be done. And so you could start to get a feel for, you know, for every hospital admission, how many doctors visits are out there where someone went to see a physician and dealt with the problem that way, rather than letting it fester and then end up in the hospital.

DR. KLEINMAN: Okay, I would like to return to the

question that was posed, which is where do we feel that PM question should be in terms of the priority within the Tier. First of all, should it be in Tier 1, 2, 3?

DR. THURSTON: Well, I would say, based on doing this review, that it should be in Tier 1. It should be a high priority. The fact that we have some uncertainty about the particular component or the mechanism, you know, we don't really know all the mechanisms. Of course, we don't know the mechanism for asthma and we don't fully understand the mechanism for tobacco smoke. And they really happen -- kids really have asthma and we don't know how that operates totally to control asthma attacks. And similarly, we don't understand how tobacco affects people fully, but certainly tobacco has adverse health effects. So I guess the point I was going to make is the fact that there's uncertainty probably means that we have to be even more prudent in the face of a risk that has uncertainty to it than you have to -- you know, public health prudence would dictate that you be very conservative in approaching this and trying protective public health even more stringently than maybe the evidence might imply because you don't really understand the problem as well and you want to make sure to protect the public health. And certainly the evidence that we have here

indicates that children are an especially affected group and that when we look at the PM standard, I would say especially the annual number is the least protective presently. You know .65, our experience in the East Coast is more like .8. And I would think in the urban areas it would be even higher perhaps than .65, the ratio. And I don't have California data. Maybe someone from ARB knows this ratio for California. Of course, it's going to vary from locale to locale, but I should think at least .65, so that when you compare that with what I'm seeing in effects at levels where the annual or multi-year means are on the order of 12 micrograms per meter cubed as PM-2.5. You know, that's the component. The other part, the short term, requires a lot more examination. And I really didn't get into that too much because usually the investigators don't give you that kind of information about what the highest or second highest is in the study, unfortunately. The distribution of the pollution is not -- you know, they might give an inter-quartile range which really doesn't tell you about the second highest or the highest. Occasionally there's a maximum and I've tried to note that. So that part of the standard really requires a look at what is the distribution of PM-2.5 and PM-10 in California vis a vis the

distributions in the studies that are available. And I think that will require perhaps obtaining the original pollution data from the researchers, who are probably willing to give it to you, or asking them to tell you what the highest and second highest were. So that information, I think, needs to be fleshed out in the process of setting the standard -- what was the distribution of the PM concentrations in each of these studies that you're looking at, so that you can compare it with the standard. And of course, you know, when you compare that standard -- the federal standard, I mean, if you're going to compare it with the federal as a touchstone, that's a three-year average, right, whereas the California is an annual. Right? Yeah. So that makes a difference when you make a comparison, especially with the short-term standard. If you're going to average over three years, the second highest is going to be quite different from a one-year second highest.

DR. KLEINMAN: Thank you, George. Also, just in going around the table, since the Recorder probably had a hard time picking up the nods of heads, it seemed that there was general agreement that the PM should be given a very high priority within Tier 1. And although we didn't ask the question directly, there didn't seem to be any real feeling

-- negative feeling -- about whether of not folding in the sulfates. So it seems to make sense to consider the sulfate and the PM standards together during that process. Is that agreeable to everybody? Any objections to having that statement in the record? Okay.

DR. LIPSETT: This is Michael Lipsett. Just a point of clarification. Are you talking about doing a concomitant review of sulfate with PM, or actually dropping the sulfate standard and folding it in within the PM standard?

DR. KLEINMAN: We don't recommend standards. No, but concomitant review would be appropriate.

DR. PRASAD: I'm assuming that means leaving the option open that it could be folded into the PM-10 standard?

DR. KLEINMAN: That would be --

DR. PRASAD: I mean is that what, Mike, your view was? Were you referring that just do the review together and still keep that option open as the review progresses and make that decision at that point of time?

DR. LIPSETT: Right, the latter.

DR. PRASAD: Thanks.

DR. KLEINMAN: I think that would make sense. And I think this brings us to the time for our break. So there

will be coffee outside, I believe. We'll be back at 11:00.

(Off the record.)

(Back on the record.)

DR. KLEINMAN: We're back and we'll reconvene this meeting. So we're going to change the original agenda and we're going to address the issue of lead. And, Bart, are you going to present the summary as well as be the chief discussant?

DR. OSTRO: Yes.

DR. KLEINMAN: Very good.

DR. OSTRO: Okay, the current lead standard in California is 1.25 micrograms per cubic meter monthly average, as opposed to 1.25 quarterly average for U.S. E.P.A. And our summary of the literature indicated that lead at current ambient levels is likely linked with neurodevelopmental effects in children, including things like acute and cardiovascular effects in adults. The indicators we usually use are blood lead concentrations and our review when we consider lead as a toxic air contaminant supported the CDC level of concern of 10 micrograms per deciliter of blood lead as a level of concern. And currently, roughly two or three percent of children below age seven are above 10 micrograms per deciliter. And if you

look at sub-populations, African American children are about six or seven percent above 10 micrograms per deciliter. And if you look at, say, African American children in pre-1950 homes, then you get numbers like 15 or 20 percent are above 10 micrograms per deciliter. So even though ambient lead is a relatively low contributor to blood lead at this point, there still would be a concern that additional lead into the air would increase the number of children above the CDC level of concern, and also possibly put adults at risk in terms of cardiovascular effects, as well as now there's some reproductive effects that's coming out from the literature. So when we looked at the five different criteria, we did think that there was a concern that we shouldn't have more ambient lead in the air. However, when you look at the exposure levels, the current ambient levels are very low relative to the standard. And another factor to weigh into the discussion is that several years ago we reviewed lead to be included as a air toxicant under the Air Toxics Program. OEHHA recommended that lead be declared an air toxicant and that local sources should be controlled under that program. It's now in the risk management phase at ARB and there was a workshop just a week or so ago in which some actual ambient levels were recommended which were well below the

standard, something around .3, I think, for stationary sources. And those levels probably will be adopted or at least put out as recommendations for the local districts relatively soon. So when we reviewed lead as an ambient standard, we thought that since the levels were low relative to the standard and that the Air Toxics Program should be controlling some of the local sources, that we therefore put it in a Tier 2 priority. As I said, we are concerned about the effects of lead in the environment from air and other sources, but we thought that it wouldn't be a priority for review at this point in time.

DR. KLEINMAN: Okay. Comments from the group? Bart, I just had a question. In the report you talk about the fact that we don't have very much data for kids in California, and that you did a sensitivity analysis from the Anne Haines. Could you explain that a little more in detail?

DR. OSTRO: Sure. The question is whether we have a representative database for blood lead distributions in the State. Typically, the blood leads are convenient samples where they're sometimes requirements for lower income children to have blood lead reported during regular check-up's. Actually, there's a strong suggestion that they

be checked-up at an early age. So there's sometimes studies like that. There have been some studies conducted from health maintenance organizations where they collect blood leads. But when we reviewed all the different sources of blood lead data for the state, we thought none of them were particularly representative of the State as a whole. They were all targeting certain populations -- either low income children or maybe where there was a hot spot and some blood lead was taken at a certain location, or from HMO data. So consequently, we thought that the national data, the Anne Haines data, the National Health and Nutrition Examination Survey, a nationally representative database conducted by CDC, probably gave us a pretty good representation of what California would be. I mean, one could argue that the means might be a little lower than the East Coast, but they're going to be higher than lots of other areas. We do have several sources here. We had a lot of cars putting out lead for many years, so the lead gets retained. So we thought in general that the distribution would be fairly similar to that described by Anne Haines 3. So then the question is what do you do with the mean in the standard deviation. So you have a log normal distribution of blood lead which is adequately characterized by the mean in the geometric

standard deviation. When you have those two aspects, you can then describe how many children will be expected to be above 10 micrograms per deciliter. So what we did in our analysis, both when we considered lead as a toxic air contaminant, as well as in our report here, was look at different levels of the mean and the GSD -- reasonable levels to see what happens if you do change the mean in the standard deviation in a reasonable way, presupposing that the distribution will be different than the national levels, and see what that means in terms of the number of kids that would be above 10 micrograms per deciliter. So you change the mean in the standard deviation and you then have a different baseline level of number of children. And it turns out that the baseline level of children above 10 micrograms per deciliter is relatively insensitive to the assumptions of the mean in the GSD within the reasonable range. And likewise, when you go from current ambient levels which are low up to higher levels as you approach the 1.25 standard, you can then look at how many additional kids would be moved above the 10 microgram per deciliter blood level -- the CDC level of concern. And likewise, there's some difference, but it's not a huge difference, it might be 40 percent vs. 50 percent, 40 vs. 45, but roughly you get

similar results independent of what the initial assumption is about the baseline distribution. So that was the sensitivity analysis we conducted. We showed that with any kind of distribution basically going up to 1.25, or even in fact going up to .5 micrograms per cubic meter, would drive a lot of children above 10 micrograms, maybe 30-40 percent above the level of concern. So that's what we did there.

DR. KLEINMAN: Shankar?

DR. PRASAD: Bart, there has been some people who are working with the lead in - Lead-Safe California and such groups -- who say that 10 micrograms as a level of concern is not the right approach in recent years. There actually is -- we show that even if you go -- it's almost like [inaudible] if any amount of lead is going to have that aspect of it. That being the dataset, somewhat the datasets are showing that, especially the learning capabilities in that part. How do you want to address that issue?

DR. OSTRO: Well, I think those concerns are legitimate. Our own review a few years ago indicated that there was really no evidence of a threshold. And there have been additional studies over the last couple of years as the blood lead levels go lower. The studies are looking at those lower levels and they're finding certainly that the

dose response relating to I.Q. effects or neurodevelopmental effects in general seem to continue at those lower levels. And there are also some studies now indicating that the effects persist into high school years. There are some studies indicating that things like high school attendance, anger, anger management, dropping out of school, general behavior problems in high school seem to be relating to blood lead, at earlier ages as well. So there's a lot more evidence coming out, you're right. And there doesn't seem to be a clear threshold in that effect. The effects seem to be occurring at lower and lower levels.

DR. PRASAD: Since you say that it's a localized problem most often and probably true, and none of these current levels are expected -- the inhalation route is not likely to be the primary source, have you given any thought of should we even have a lead standard as an ambient standard as opposed to we just control it as toxics? I mean, for the sake of if we are really not doing anything specific except for the sake of -- I mean, the reason I'm asking that is, the moment you say that you have a standard, you have the right to monitor. And that is a resource issue and a personal issue, and as far as I know, I think it is for the sake of lead alone that TSP is still monitored

because they don't measure lead from the PM-10 sample, but use the TSP sample in some of the locations. So that's a huge resource issue. Are you going to -- whether you address it in a Tier 1 or Tier 2, it doesn't matter as maybe some [inaudible] has to whenever that standard is reviewed, probably serious thought should be given to that aspect of whether it is continuing to have that kind of a standard.

DR. OSTRO: Yeah. I think that's really not in my purview. I can tell you what I think the health effects are relating to it, but in terms of whether the standard should exist or not I think is a joint decision with your office as well. I think there is an issue about what message it sends out to other States and other countries, even, in terms of whether we should keep a standard of 1.25, which is clearly not protective, lower, or get rid of it totally. So I think all those things have to be weighed.

DR. KLEINMAN: Shankar, I'm not quite sure whether it's true that the ambient air concentrations are not reflected in changes in blood lead.

DR. PRASAD: I mean, from the exposure part, from the levels that are observed, that's the kind of feeling I hear from the people that worked on this, that the ambient levels alone would not lead them to such high concentrations

at current exposure levels. It's more driven by the condition of a very high source part of it, which we do not pick up by the ambient measurements, unless you do defense line monitoring of specific sources, and so on. That's why -- that's how I was saying that you have a toxics program which would focus on those areas, potential hot spots and emission sources, and trying to set up those kinds of limitations and control technologies, and focus at those sites vs. really an overall monitoring network for the whole state.

DR. OSTRO: But we do find that there's a pretty good accordance with ambient lead and blood lead. I mean, as one changes the other changes over time pretty well. And all the studies that we looked at showed that changes in ambient lead will affect blood lead in a significant way.

DR. KLEINMAN: Varo?

DR. VOSTAL: Although I would completely as a private citizen say that since we have a standard, there could be really in the future some possibility that there could be some local sources which will come again. It's good to keep it on. Otherwise, I agree with the position of ARB. The contribution of the intake of lead to the respiratory system is very low, even for adults, as well as

for the kids. In comparison with that, the SUR really correctly stated in the outline there that the kids are much more sensitive to the [inaudible] intake of the lead since in the small children there is practically more than 60 percent of the metals up short from the gastrointestinal system. From the respiratory system, it could be as low as about ten persons. So from this point of view, this is always really a concern. I have seen this situation with the lead exposures in Europe and I have seen it here. We have been always asking the question why don't we see the impact on the children in Europe as it has been described here very frequently in 1950's and 60's in the United States. And only when I came to the United States, I have discovered that this is due to the fact that most of the exposure for those children who were influenced by the high blood level considerations was coming from a completely different source. That means from the lead pigment in the paint. The people in Europe are not really using the lead in the paint, and they are not painting their houses, you know, with white as it is being here, therefore the situation was they're much better. And although they were using the cars with the emissions of the leaded gasoline, you know, the exposures were not as profound that they could

really produce some effects which we have seen here in the United States. So that's really from the point of view it's very clear, I suppose, that we are still much more concerned that the amounts of lead which could be taken by the kids from other sources are probably much more important than the exposure to the air. And if I can have a question, if you could return to the first slide, you are saying that it's probably linked with a neuro-effect in the children and with the cardiovascular effects in adults. I have not found any of it about the cardiovascular effects discussed in the report. Could you tell me what is the information for this statement based on?

DR. OSTRO: Yeah. The cardiovascular effects weren't discussed that much in the report because we were focusing more on the children effects. And we thought the effects were at lower levels for children and probably more relevance for SB25. But there's probably been about a dozen studies now relating blood lead to diastolic blood pressure and hypertension. So E.P.A. has conducted several reports on that and it's gone through their own KSAC review suggesting that they agree with several metal analyses that have been conducted showing that blood lead relates to various cardiovascular effects in adults.

DR. VOSTAL: If I may, I think that you are right and therefore I ask it, it has really been discussed long time ago in the first declarations of the scientific basis for the federal standard and so on. But since that time, I suppose that we have realized that many of those things were done on the relatively weak assumptions. And they have not realized it was mainly based on the calculating effects and we have never seen it. I have seen many people occupationally exposed to the lead, and only in those who were exposed to very high concentrations, we were addressing ourselves to if there is some relation to the cardiovascular effects. But we have never been 100 percent sure about it.

DR. OSTRO: We looked at both the occupational and non-occupational studies. Certainly occupational exposures are much higher than the ambient exposures, but even when you look at normal ambient exposures to adults, where the means are say in earlier years maybe around 8-10 or 12 micrograms per deciliter, they found pretty good associations with cardiovascular outcomes. So even the non-occupational exposures seem to be there. Also, one other thing about the children's studies mean most of the cohort studies have been conducted in the U.S. and in Australia where these studies have gone on for about 15 years, and

they've been following children populations. But there is some studies in Eastern Europe that are coming up when we go to the I.S.E.E. meetings. More and more studies are coming out. And I think there's a cohort actually from the Czech Republic showing similar types of effects on children in terms of I.Q. I think there's some studies now from Hong Kong and from other places showing similar types of neuro-developmental effects on children.

DR. KLEINMAN: There are also -- going back to the cardiovascular effects -- there are studies done with animal studies showing kidney toxicity leading to hypertension. And these have been followed-up clinically with humans and there does seem to be a fairly good association there.

DR. OSTRO: So I guess one of the questions for the reviewers here is whether they support our recommendation of keeping lead in Tier 2, even though we do think there are significant health effects of concern, given the current ambient levels and the Toxic Air Contaminant Program, whether you would agree with us that it be a Tier 2 pollutant at this point.

DR. KLEINMAN: Comments from the committee? Mary is indicating yes.

DR. WHITE: Yes, this is Mary White. I think

that's a smart move.

DR. KLEINMAN: Yeah, I think keeping it in Tier 2 makes sense given the low ambient concentrations and the reduction in source emissions for lead at the present time. There was one interesting article which I don't know how good the science was -- I think it was an interesting think piece -- indicating that if we pushed for the zero-emission vehicles, this would cause us to need far more lead batteries than we're currently using, and that the amount of lead emitted during smeltering and processing operations might exceed the amount of lead that was previously emitted from leaded gasoline. Again, this is just an article based on computer modeling and things like that. There were no real data that were taken. But it's an interesting concept. Some of the things that we do for regulation have unforeseen effects. We've seen that before with MTBE, for example. At any rate, I think the lead standard as an ambient standard might have an important value to hold the line, certainly, and keeping it in Tier 2 makes sense to me. Kent?

DR. PINKERTON: I would also agree that keeping it in Tier 2 seems very logical. The question I have is how routinely is lead a component that's measured in the

different monitoring sites around the State? Is that something that is done at all sites, or is that archived so that that can be measured at future dates?

MR. WESTERDAHL: Dane Westerdahl again. Lead is not measured at hardly any of the sites in California at this time. There are requirements based on federal standards as well as State standards that require us to do some monitoring. As was mentioned earlier, the methods that we use as far as the median techniques are defined in those standards and in both cases they're different than routine monitoring methods. There's a great deal of PM-10 and 2.5 monitoring going on in the State on a routine basis. The methods don't coincide with what's required to do routine lead monitoring, so we don't have a great deal of ambient lead monitoring in the State. I think that was your question, right?

DR. PINKERTON: Yes.

MR. WESTERDAHL: And one of the things that you've heard mentioned is that, as the standard might be reviewed, we might reconsider so that we could use PM-10 or 2.5 samplers in samples to do lead analyses. Lead is considered in part of our toxic air contaminants monitoring network. There are in fact -- Mike, does anyone know how many toxics

or contaminant stations there are in the State? I think it's on the order of 20-30. Twenty? And at those stations, lead is being collected on an every one and 12 day frequency. And it's done by a different method than ambient air quality standards call for.

DR. THURSTON: Dane, I have a question. The E.P.A. speciation network will be starting up sites throughout the nation and I would guess that they're going to analyze the samples by XRF which gives you lead. Isn't that right?

MR. WESTERDAHL: That's correct.

DR. THURSTON: So won't we get a lot more lead information as it -- how many sites do you think will be in California?

MR. WESTERDAHL: As I recall, it'll be a couple dozen at least. Now again, that will be by a separate method. XRF from the speciation will be done on 2.5 size cut, so some of our lead samples come from TSP, some may come from PM-10, some will come from 2.5 and the speciation --

DR. THURSTON: Is there some reason to believe that that's not all going to give you basically the same answer?

MR. WESTERDAHL: Different size cuts are going to give you different answers, possibly, but lead should be in the final fraction --

DR. THURSTON: That should be in the sub-micron, yeah.

MR. WESTERDAHL: -- unless it's resuspended contaminated soil.

DR. THURSTON: Rats -- from rodents, could be, yeah.

MR. WESTERDAHL: So there may be a difference there and there are differences in the sensitivity and the base methods themselves help describe the values you will report. They shouldn't be comparable.

DR. THURSTON: Well perhaps there should be some work done side by side if this hasn't been done already to evaluate comparability so that it can be used for standard setting appropriately.

MR. WESTERDAHL: I think our monitoring laboratory division would be interested in that because it is quite a workload for them to do -- to help support these various kinds of ways of collecting similar information. So they might be convinced to do some comparative studies.

DR. KLEINMAN: Any other comments? We have about

ten minutes before we break for lunch and it might be useful in case someone had to leave early and had some comments on any of the other pollutants that they wanted to make that they would have made during the public speaking session at 1:00 or 1:45, if they'd like to make those now. Jaro?

DR. VOSTAL: I think this is related directly to the question which was asked how much of the lead is even in the PM-2.5 fraction. And the studies have been done on the speciations so far in some selected states. And I have here the results from Texas where, out of the 17 micrograms of the PM-2.5, it was only .006 nanograms of lead in the fraction of the PM-2.5. And so maybe this is --

DR. THURSTON: Jaro, I'm sorry, it's George Thurston. I didn't understand the percentage was what? You were looking at PM-2.5.

DR. VOSTAL: PM-2.5 and it is expressed as micrograms per cubic meter. And the concentration for lead in the PM-2.5 is only .006 microgram.

DR. THURSTON: Well, but the question really was how much of the TSP lead is in 2.5.

DR. VOSTAL: TSP --

DR. THURSTON: TSP, the total suspended particle -- how much of the total lead in the air is in the sub-2.5

micron fraction?

DR. VOSTAL: All that I wanted to tell you was that the concentration in the PM-2.5 is very low, I don't know how to compare it. But as you have seen in view that there is a very low concentration, only .06, in the measure even in California. So those levels are very low.

DR. THURSTON: I'd have to go back and look at my dissertation, but I remember analyzing the six city dataset for trace elements, and virtually all of the lead -- you know, they had two fractions -- less than 15 microns down to 2.5, and then 2.5 and less. And my recollection is that the vast majority, certainly well over 90 percent, was in sub-2.5.

DR. VOSTAL: But what year was it?

DR. THURSTON: Oh, yes, sure, that was when leaded gasoline was used.

DR. VOSTAL: This is what I would expect, yes. But not now.

DR. THURSTON: Yeah, well maybe re-suspension would be a bigger percentage now of a lower number.

DR. VOSTAL: But the resuspended probably will be appearing more in the larger coarse fraction than in the PM-2.5.

DR. THURSTON: Right, but then that would be -- maybe it wouldn't get into the deep lung, but it would be swallowed. So you'd still get it in your system.

DR. VOSTAL: Yes. But fortunately when we are, you know, in adults it doesn't really make such a difference since we are practically not observing too much of the lead from our G.I. tract, only the children. But if you feel that this could really be a significant contribution, maybe it is an important relationship to the direct standard. But let me try to explain a little more the discussion about the PM. And some of the you have already heard -- the question is, if we can really look how to validate the statistical associations coming from the epidemiologic reports, can we find out if there is some substrate which will help us to confirm that there could really be those effects due to the larger considerations of PM-2.5. Now the lung [inaudible] has been really in effect since 1960's for more than 30 years, but it was the International Committee for the Radiation Protection which just recently came up with a new way of how to model the possibility of the particles deposited in the lung. So just only to find out from some preliminary estimates how much it could really be attributed to the question of the toxicity of PM-2.5. We have tried to

apply -- it's coming from two cities in the United States which were providing the distribution of the particle sizes and we have done some calculation. As you can see it, we used the data from the Texas study where the annual consideration of PM-2.5 was at the level of about 17.5 micrograms per cubic meter. We have calculated how much it could really be inhaled by the adult person. It could really be corrected even for the children and so on. And you can see that the inhaled dose of the toxic metals -- this is what we are really, as we have heard from the discussion before, you know, probably more concentrated more on it is only one-third of the microgram per 24 hours. Now we have said that if the time series are correlating the 24 hour inhalation of the PM-2.5 with the daily mortality, then it would be important for us. What is the amount of the potential toxic components which are retained in the lung which could be responsible for that effect? Now it is calculated for the -- since it is PM-2.5 which is expected to penetrate deeply into the respiratory system, so we calculated amounts based on the two -- one for the city of Philadelphia, one of the city of Phoenix. And as you can see, when it comes to -- again, this is calculated from the ICR 6 to [inaudible] 1,100 micrograms and then you can see

that in nanograms, in per gram of the tissue, the toxic metals represent only roughly very small fraction. It is the fraction of a nanogram. If you even do it and you calculate it on the basis of the lung surface, which seems to be much more important, then we are coming even to much lower levels. Again, it is expressed in nanograms and you can see that for the toxic metals how many zeros we have to come to it and that means that there will be [inaudible] 24 centigrams, which is 10 to the minus 15 of a gram. So those are really levels which are surprisingly very low to be responsible for such a complex effect as the mortality or morbidity. And it doesn't seem that it's too much constituting to the fact that we can really -- that there is a real causal relationship that means it is the amount of the fine particles which is retained in the respiratory system which is responsible for the effect. But still, it doesn't help us, it doesn't tell us what is responsible. It could still be that the PM-2.5 as it is used by the federal E.P.A. should be only considered as a surrogate which might really be indicating for us something, but we have to study more before we can really conclude what the real public health impact of it is. So this is really what I wanted to say.

DR. THURSTON: This is George Thurston. If I could just comment, I mean, I think that there are two alternative hypotheses that you could go to from the calculations that you've done. And that is 1) that the PM effect is implausible, which is what you're, I guess, saying, and the other is that PM is very toxic. Ambient particles coming from combustion sources, burning coal and oil are indeed very toxic. And since you don't have a reference as to what's the level required for a health effect, I don't think that this really answers the question which one of those two hypotheses is correct.

DR. VOSTAL: That's great, George. You are answering nearly the same way as Mort Lippmann when we were discussing the ozone. And he said, "When I look on the ozone issue, then I am seeing the bottle which is half full. When Jaro is looking on it, it is really half empty." So obviously --

DR. THURSTON: I don't think he made that one up though --

DR. VOSTAL: Excuse me?

DR. THURSTON: The half full, half empty analogy -- I don't think he made that one up.

DR. VOSTAL: But he has used it and it is

published, so you know, I agree with you. It is not really the way. We are looking only for things which could be separating our hypothesis. Now we are having a big problem to find a plausible explanation of these very low concentrations to be responsible for such a complex effect as mortality.

DR. KLEINMAN: Can I take the Chair's prerogative to take the last word and then break for lunch? And that's going to be to say that one of the things that you don't include in that smearing out of the deposition across the entire surface area of the lung is that the particles don't deposit uniformly, they deposit in selected locations based on the particle size. And if you look at the deposition pattern in selected parts of the tissue, there can be thousands of times more material deposited in a very small localized area, and therefore that's going to change the way the toxicity works in that area. We've seen that in animal studies where you look at localized regions and you see regions of damage. And let's break for lunch --

DR. VOSTAL: If I may just only answer --

DR. LIPSETT: Actually, Mr. Chairman, I wanted to see if you would mind waiting to break for lunch until Mary White could make some comments about the prioritization

because she has a plane to catch at 3:00, so she will have to leave probably right after lunch.

DR. KLEINMAN: Okay. I wanted to also ask, do you know when John Balmes is getting back?

DR. LIPSETT: He'll be back during lunch.

DR. KLEINMAN: During lunch. What I was going to suggest is we might want to abbreviate lunch or eat during -- for the discussions. But if he's not here, let's just let Mary go ahead with her comment and break.

DR. WHITE: Well, Mike was generous enough to offer me this potential option, because the other option gets me back pretty late. Well I wanted to say that I was very impressed at the quality of the reviews that were sent to us. And I thought it was extremely helpful. I'm very comfortable with the Tier approach that's been proposed. I think it's completely appropriate to put the pollutants in Tier 1 and Tier 2 as have been proposed. My reading of the reviews -- in my mind, it's very clear that there is substantial evidence that at current levels of exposure, both particulate matter and ozone are causing adverse effects to children, that you cannot possibly look at this evidence and not conclude that this is a risk, and that more needs to be done to protect children. But I come back to

the idea that there's this difference between the current standards and current exposures. And I would be comfortable with either particulate matter or ozone being selected as the first pollutant to review. I think either one would be a fine choice. And the only reason that I wouldn't just say, "Go after particulate matter first," is that I come back to the concern that I wouldn't want to have a lot of effort go into reviewing a standard if that standard wouldn't materially impact actual exposures. So if it were possible to consider a standard in a way that would stimulate re-thinking about control strategies or whatever, that at the end of the day, you've actually materially reduced exposure to children, then you would have succeeded in your ultimate purpose.

DR. SHERWIN: Michael, may I make one quick comment?

DR. KLEINMAN: Quick.

DR. SHERWIN: There's a very basic pathobiologic principle that's being overlooked when you talk about diluting out the particulates. In my study with the particulates from the vineyard workers, the thing that impressed me very much was the fact that macrophages picked up those particulates. Those particulates, I thought, had

absorbed some kind of a toxic substance. And the macrophages release a lot of hydrolyses. And to me, the fundamental harm that I see in those particulates and which I suspect in others, is hydrolates release from macrophages. Now that principle, incidentally, has been the fundamental principle of the cause of interstitial pulmonary fibrosis. And it is injury to the macrophage that causes IPF. So this idea of diffusing the toxin over the epithelium is not in accord with the information that I know, nor my personal observations. The problem is the macrophage -- picking up, concentrating this material, and then releasing very noxious hydrolase.

DR. KLEINMAN: Good point. Do we have lunch? We have lunch.

(Off the record.)

(Back on the record.)

DR. KLEINMAN: All right, we're in the home stretch. Our topic is now going to be carbon monoxide. And I believe -- Bart, are you going to do the summary? And then I think Bart is also going to moderate the discussion session? Oh, John is going to moderate.

DR. BALMES: Take it away, Bart.

DR. OSTRO: Thank you. Okay, our eighth and last

state ambient air quality standard is carbon monoxide. And we put carbon monoxide in the Tier 2 category. So a quick review. Our summary stated that there are three standards in California. There's a one-hour, an eight-hour, and an eight-hour high altitude Lake Tahoe standard. And the current standard is based on protecting people with coronary artery disease. And the basic end point was decreased exercise time to angina based on several carefully controlled studies that were done. We reviewed this again a few years ago and basically agreed with the similar conclusions that the standards as we recommended them of 20 ppm and 9 ppm were protective. Those levels are lower than the federal standard for the one hour. When we looked at the actual concentrations in California, they're generally low relative to the current standard with the exception of two sites. One of them is in Central L.A., which always seems to show high CO levels. And last time I talked to ARB about it, they were doing some analysis to try to figure out why that site always tended to be a hot spot. I don't know if they ever came up with a conclusion on that. So our summary indicates that we think the standards generally appear protective based on the controlled exposure studies of people with cardiovascular disease. The U.S. E.P.A. just

finished their own review and published it a couple weeks ago -- about a month ago. And their review of both the controlled studies and the epi studies also seemed to indicate -- or did indicate -- that they believe that their current standards are protective of public health. And I think the newest wrinkle to this issue has been some of the epi studies that have come out over the last two or three years. There's been now several studies that are showing relationships between carbon monoxide and hospitalization for cardiovascular disease. And there was also a study recently that came out that showed relationships between carbon monoxide and birth weight in Los Angeles. And as we indicate on the slide here, these studies are generally well conducted, but problematic in terms of assigning a role to carbon monoxide, basically because the monitoring of carbon monoxide is not very representative of what the population exposure to carbon monoxide would be, and also because carbon monoxide is correlated highly with some of the other traffic related pollutants. So I think the general assessment of E.P.A., as well as OEHHA, has been that it's hard to or difficult to assign a specific effect for carbon monoxide. So based on the fact that the controlled studies appear reasonably protective, the epi studies are somewhat

uncertain, and that the current concentrations are generally for most of the State lower than the standard, we put this pollutant as a Tier 2 pollutant.

DR. BALMES: Mike, do you have anything to add?

DR. KLEINMAN: One on the point of the fact that carbon monoxide measurements are not -- or carbon monoxide exposures are not well represented by ambient air monitoring, that's sort of a general argument. And you could make about the same case for PM where you look at the personal cloud and the personal measurements are invariably higher than that predicted from either micro environmental monitoring or even for ambient air monitoring. I think the key thing that we have to look at is that these epidemiological studies which are fairly recent now, that are beginning to show some of these effects, are very suggestive and they're at least as suggestive for an effective seal on fetal toxicity as PM measurements are suggestive of mortality effects, I would think, although they're nowhere near the number of studies that have been done on this topic. So I wouldn't dismiss them out of hand. Another issue is the issue of dosimetry, especially for children. Children have a more rapid ventilation rate. And although there's not a whole lot known about the affinity of

fetal hemoglobin for CO per se -- there haven't been many studies of that -- if you just assume that the hemoglobin affinities are the same as in adults, it takes about ten percent less CO exposure for a kid at rest to achieve the two percent carboxyl hemoglobin level that is used as the basis for setting the ambient air standard. So at least on their breathing perimeters, CO is about ten percent. They'll have ten percent higher exposures than a comparable adult. This is worsened in kids who have inflammatory lung diseases. There are some studies that indicate that their baseline carboxyl hemoglobin levels, which in a normal individual might be as low as a half a percent or maybe even lower. There aren't very many good data points on carboxyl hemoglobin in kids. But the kids with inflammatory lung disease like asthma can have carboxyl hemoglobin levels as high as one percent as a normal average. And obviously, if you're starting at one percent, to get to two percent it takes less external carbon monoxide. And the graph that I put into the chapter which I should have made the legend a little bit more explicit, but I think it makes the point that it takes less inhaled CO for a kid with an inflammatory lung disease, which could include a temporary situation like a lung infection to achieve the two percent level that would

be considered problematic. So from those standpoints, I think that CO is worthy of consideration. I don't think it means that we need to move it from Tier 2 to Tier 1, but I think within Tier 2, it should be given a relatively high priority.

DR. BALMES: Any other comments from the committee? Shankar?

DR. PRASAD: Any thoughts, Mike or George, in terms of this CO is also a surrogate of combustion sources. That's been also speculated as opposed to saying that most of the effects observed are attributable to PM, but CO is a better surrogate. Do you have any thoughts?

DR. THURSTON: Well, I guess there are those who say if you're seeing the CO effect or association, shall I say, that that might be a marker for particles of transportation -- cars and trucks. So again, it comes down to trying to choose there. At least from the epidemiologic perspective, it's hard to separate out whether it's a CO effect or a PM from let's say diesel trucks and so forth contributing to the PM mix. So I think we'll only know the answer to that when we start getting at tracers in the particles, looking at carbon over time and other tracers of automotive and truck particles and see if they correlate as

well as the CO or not in trying to separate out that. But I think we don't have an answer to that right now.

DR. KLEINMAN: There is the one Ritz and Yu paper that both you and I cite, in which they did not find a correlation with TSP and reduced birth weights, but they did find a significant association with CO.

DR. THURSTON: Right, but TSP is not very useful.

DR. KLEINMAN: Well, it's not a great marker, but it does indicate that perhaps the CO acts alone, plus under other conditions -- tobacco smoke, which is quite high in CO -- has similar effects on birth weight and in animal studies, CO alone can produce birth weight changes. So there's a biological plausibility to it. And reduction of oxygen delivery to mothers, for example by having them at a high altitude during pregnancy, also is associated with low birth weight. So CO reduces oxygen delivery. Low oxygen is associated with -- there's some good biological plausibility to think that this may be reasonable. It's certainly not proof, but it's at least along the lines of having some mechanistic back-up for it.

DR. BALMES: Any other comments? Russ?

DR. SHERWIN: Yes, just a question really. I wonder if somebody would update me on relative levels of CO

on the highway in a car in traffic, as opposed to ambient. I know there's data on that, but I don't have an update in my mind and wondered if it's possible that the standard would be more relevant for indoor driving than outdoor air. I'm not sure. What is the latest on that? Anybody know?

DR. KLEINMAN: The data that I've seen indicates that the levels indoors and in vehicles are exactly the same as the levels outside a vehicle. There's almost no scrubbing of the CO by the vehicle itself, you know, in a home. So CO levels indoors and outdoors are pretty comparable. So to the extent that epidemiology is measuring effects associated with outdoor air exposure, the CO should be as good as anything else. But on the freeway, it's probably high.

DR. SHERWIN: I had in the back of my mind that sometimes air circulation in the car, if somebody inadvertently turns off the circulator, for example, as you sometimes do and you get behind a diesel and you turn off all the air, if you happen to have a high CO in there, it's going to last a lot longer than outside. So the question is not just level but dosage.

DR. KLEINMAN: Co turns over very quickly because it's such a small molecule, it diffuses rapidly. But

vehicles, you know, that's such a specialized market. How many cases do we have per year of kids riding in the back of a car and CO being sucked in from the exhaust just because of the Vender [phonetic] effect creating a vacuum behind the vehicle?

DR. SHERWIN: But that's what I had in mind --

DR. KLEINMAN: So vehicles per se may be, you know, if they're malfunctioning can be quite high.

DR. SHERWIN: But how about the car in front of you, which is what I had in mind? That you're behind a car and it's giving you a lot of CO, and you take in a concentrated dose? That's got to be more than what's being diluted outside. DR. KLEINMAN: I'm sure it's indeed high.

DR. SHERWIN: The big question is hard data. Maybe Dane has hard data.

MR. WESTERDAHL: Dane Westerdahl again. On that specific case, maybe I can clear that up a bit. And Mike will jump in, I'm sure, to clarify it. For CO, it's not a rapid toxicity sort of thing. The car in front of you is going to be in front of you for minutes, or ten's of minutes. Your absorption of CO is a relatively slow process. And so there will be an impact on your overall

blood CO HB levels, but not a huge impact. There are higher CO levels on the freeways -- on the highway than there is near the highway because that is a major source. So you will have an elevated exposure, but you soak it up fairly slowly. It will impact your overall levels, but it's a fairly slow impact.

DR. SHERWIN: Well, don't forget, those of us in Los Angeles are behind these cars for 30 minutes, an hour, I'm on roads --

DR. BALMES: Mike will explain that.

DR. KLEINMAN: Well, I can give you data that's been produced by -- dare I mention Areno's name? But Areno did studies of people driving in freeway traffic and driving approximately one hour on a congested freeway raised carboxyl hemoglobin levels from baseline to approximately 2 - 2.5 percent.

DR. BALMES: And those were in the days before catalysts were in the cars.

DR. KLEINMAN: And that was before catalysts. So the levels are probably less drastic now, except for exceptional cases.

DR. BALMES: The data actually does exist and maybe we can get a little bit to Mike to include on --

DR. KLEINMAN: That would be useful. I'd appreciate that.

DR. PRASAD: Dane, just a -- do you make a study that [inaudible] Group did the measure of CO? I mean, you remember they did actually a study of both inside the vehicles, outside the vehicles, and they ran some materials as well as the freeways in Los Angeles just around two years back. I didn't see that CO was showing up anything big, but I'm not too sure about that.

MR. WESTERDAHL: The major findings of the study that you mentioned was done under contract for Air Resources Board was on particle exposure, particulate matter exposures depending on who was in front of you and how far you were from a highway, and how much traffic there was. I'm afraid I can't remember carbon monoxide measurements. Can you remember them at all? It would have made sense.

DR. PRASAD: I don't remember. That's why -- I know that there was a big PM difference when they followed a diesel truck. That's one thing I remember did come out from that.

MR. WESTERDAHL: And the point that Mike made was, or whoever made that, was it's the vehicle. The air inside, even for particle, is very much like the air of just outside

the window --

DR. PRASAD: Yes.

MR. WESTERDAHL: So it's not so much your car, it's where your car is.

DR. KLEINMAN: It's the guy in front of me that I'm --

MR. WESTERDAHL: Yeah, don't drive behind people, yeah.

DR. KLEINMAN: There was -- if I remember right, I don't know if the data were published, but Wayne Ott did some studies where he was collecting CO on freeways and driving around, and he had some data that he presented at a meeting, but I've never seen the data published. Maybe I can twist his arm and get him to publish that information.

DR. BALMES: John?

MR. HEUSS: I can maybe help clarify this a little bit. John Heuss, Air Improvement Resource. The latest CO criteria document goes through this quite extensively. And you're right, Dr. Sherwin, there's about a factor of three increase for things that are emitted on the roadway like CO, lead used to be, and so forth, in vehicle measurements. There have been a whole body of measurements -- 14 or 15 studies of CO from the 60's when we used to have 30-40 ppm

at the monitoring stations, and then commensurately higher concentrations in vehicles. But for things like Benzene and CO, which have been extensively cleaned up throughout the vehicle fleet, there's still that factor of three difference between the ambient monitor in the vehicle in congested freeway traffic, or arterial traffic. But the whole concentration distribution has dramatically reduced by at least 65-70 percent for benzene, and probably more like 90 percent over the last 20-25 years.

DR. BALMES: Thank you. Bart?

DR. OSTRO: Just some quick responses, Mike, to your comments. First of all, I agree that some of the epi studies with CO are interesting. I wouldn't say, though, that they are at the same level as the PM-10 effects studies, probably because there's a lot of other confounders for the CO and phytotoxicity effects that are not taken into account in some of those studies like parental nutrition -- mother's nutrition. And also, that study is a cross-sectional study where a lot of the PM-10 studies are time series studies so that you can really control for the confounders. But the CO and hospitalization for cardiovascular disease is interesting. It is a time series study and there are several of them. And I don't think it

can be ignored. But my understanding of the CO exposure is that when people were studying this ten years or so ago -- I think there was a group in Denver, a consulting firm that did a lot of the personal exposure studies -- they found basically no correlation between the monitors and exposures where at least you'll certainly have measurement there with particles, but you had some correlation between exposures and what the monitors were saying. So I think the epidemiological evidence is a lot stronger for the particle effects. The second thing I wanted to say was that the Beati Ritz study that you referred to and that George referred to showed effects on birth weight. There's a new study in epidemiology that came out last month showing effects on premature birth and in that study, there's very strong PM-10 effects and a little bit of a CO effect in the inland counties. But there's in a way replication, but with a different end point, but finding very strong PM-10 effects there.

DR. BALMES: Was that a Ritz paper as well?

DR. OSTRO: Yeah, same authors. And the third thing I want to mention is that, with the children with inflammatory diseases having a higher baseline level, then they only have -- in your discussion, you talk about going

up to a two percent CO HP level, but the two percent for children may not be the relevant marker. I mean, 2 or 2.5 percent is relevant for the elderly and people with heart disease, but the only effect I saw in your review and in our own review for children with maybe some of those video game effects -- a study of about 90 people single blinded -- and I don't even know if I want to worry about that -- so I don't know if 2 percent CO HP is the relevant indicator, unless you know of some other studies for children that are showing effects at those levels are indicating that.

DR. KLEINMAN: No, to my knowledge, there haven't been very many tox studies with children, essentially zero.

DR. BALMES: Any other comments or discussion? Are we finished with CO? It sounds like it.

DR. KLEINMAN: I think so. Thank you, John. So having done that, we've got a little bit of time that we can use for any additional public comment on any of the pollutants that have been discussed in the last two days. George?

DR. THURSTON: Yeah. I did have one thing that I wanted to bring up with Ira Tager about ozone that we didn't have time for. And I just sort of wanted to get it into the record, which had to do with the possible role of ozone in

induction of asthma, because I did not see in the write-up any discussion of that issue. Maybe I missed it, but I didn't see it. And I didn't see a reference to the Ashmug study where they have found in their study that higher ozone was associated with a higher prevalence of asthma. And I think that's the first study that's found that. And I think Ira is about to start a study investigating this issue -- in young people?

DR. BALMES: I'm a co-investigator of that study -- the phases study -- the FACES study -- Fresno Asthmatic Children's Environment Study. And that's actually not about the induction of asthma. We're going to recruit asthmatics and be looking at whether air pollutants are involved in exacerbations of asthma, and whether kids who get air pollutant related exacerbations have a worse course to their asthma, but it's not about induction.

DR. THURSTON: It's not about induction, okay. Well, anyway --

DR. BALMES: Ira does know -- I mean, Ira frequently discusses the Ashmug study, so it was either an oversight or he had a reason for not including it.

DR. THURSTON: I don't know. It's -- Machino is one of the authors. I think on the abstract, he was first

authored, but in the paper he was maybe second or something. But I know that's one of the authors in that paper.

DR. BALMES: I can certain bring that issue up with Ira.

DR. THURSTON: Yeah, I just wanted to make sure that that section is discussed.

DR. BALMES: That's a good point.

DR. KLEINMAN: Just to briefly summarize. From our comrades who had to leave early, Henry Gong made a brief presentation about PM and felt that PM should be rated in Tier 1 as the first priority pollutant to be investigated. Mary also felt that either ozone or PM would be appropriate. And I think it would be appropriate now to just sort of poll the committee. Is there anyone who feels that items that have been placed in Tier 2 should have been in Tier 1, or anything in Tier 1 that doesn't belong there? Tier 1 right now is PM, ozone, and NO2. Is there any feeling that any of those don't belong? Let the record show no. Is there anything else in Tier 2 that should be considered either in Tier 1 or -- all right, let's go back to Tier 1. In Tier 1, does anyone feel that ozone should be addressed before addressing the PM issue?

DR. SHERWIN: Why is it necessary to rank the two?

DR. KLEINMAN: Just to provide some record that we discussed the topic and that if --

DR. BALMES: I think it's unlikely that the agency can do both at the same time. Is that correct? And keep everybody's sanity.

DR. KLEINMAN: And to -- you know, we are the Air Quality Advisory Committee and we're supposed to give advice. So if we can advise them as to what we think. They don't necessarily listen, but we can advise them.

DR. OSTRO: Of course we listen! But under SB25, as I said yesterday in the intro, we're required by the end of this year to make a recommendation to the Board as to which pollutant we think is -- first of all, if any pollutants are not protective of public health, particularly of children and infants, but then second, of those we think that are not protective to determine which pollutant we should begin to review first. So we are interested in what the scientists in the scientific community think as the most important pollutant for review.

DR. SHERWIN: I was just concerned that we might unduly understate ozone if we pick PM-10, or vice versa. Now needless to say, a chronology can be set, but I don't think we should give the implication that one is of greater

concern than the other, but I'm perfectly willing to choose some chronology and I'd say the chronology might depend in my mind upon which one has the least dangers. I see ozone right now -- we know so much about it in my opinion, and I think we can make recommendations without any question. Now whether that should be a standard change or whether it should be just advisory is another question, but if it comes down to getting data, I would say the particulate is certainly going to be the toughest job for us. So I think it's far more complicated than is the ozone.

DR. KLEINMAN: I think it's also important to recognize that the PM-10 standard that the State has is very different from the proposed federal standards, and therefore the State really will need to review the PM standard whether we've agreed or not, and I think getting a jump on it would be to their benefit. So I would think that for a number of reasons PM is probably the issue that needs to be addressed first and it's very likely that they're going to need all of the two-year time frame that they're allotted to be able to get the data summarized and start to make decisions.

DR. BALMES: Yesterday I said you could make a case for starting with ozone and the case that I would make for ozone would be that I think we, as Russ said, have more

data from all phases of the components of the usual scientific database in terms of controlled human exposures, toxicology, and epidemiology where I think, while we have a lot of epi for PM, we don't understand biological mechanism as well. But that's the case I could make for starting with ozone. But I actually feel that it may be more important to do a review of PM just because there are more uncertainties about PM and PM is getting more sort of public attention. And the uncertainties about the PM data are getting more public attention. But I do feel think that if a decision is made to go with PM first, it's not because PM is considered sort of a worse pollutant with ozone. I agree with Russ on that point.

DR. PRASAD: I agree with you, John, but the review is not resolving uncertainties. The review would probably highlight the uncertainties. It's not supposed to reduce the uncertainties. So the issue of if the uncertainties -- the issue that we address probably [inaudible], or am I wrong in that?

DR. BALMES: No, but I think that highlighting uncertainties is not a bad thing.

DR. PINKERTON: Kent Pinkerton. I agree with many of the things that have been said today, especially in the

last few minutes. I would like to just emphasize the fact that when we speak of children and these criteria air pollutants, I think that both ozone and PM are of great importance. And so I think if we have to prioritize, I guess I would go along with what most everyone has also said, and that is to put PM-10 first. But I don't think, as John says too, that we don't want to do that to suggest that we think it is more important for children's health protection to consider only the PM issues. I think ozone is just as important an issue as PM is, but if they can only do one pollutant at a time, then perhaps that decision needs to be made that would be most timely for what's happening in the rest of the nation and the world. However, it is interesting, not from a scientific perspective, but just from a local perspective, in the last two weeks in Sacramento we had an article in the Sacramento Bee that was talking about children's health and air pollutants, and it said nothing about PM. It was totally on ozone. Now how they arrived at those conclusions that children's asthma in Sacramento is driven by ozone, I'm not sure exactly what the scientific basis is for that.

DR. BALMES: I can answer that possibly. It's because -- Michael is not here so I can speak -- he gave an

abstract -- he and a colleague gave an abstract -- relating what MediCal admissions to the hospital in Sacramento and ozone. And I think the paper found out about it and, even though it was an abstract and hasn't even been written up yet, decided to report it on the front page of the paper. So I think that's what drove the ozone interest in Sacramento. Correction here?

DR. LIPSETT: Well, yeah. The Reporter was well aware that this report had not even been subject to internal peer review yet. I mean, it had been presented in abstract form at ATS and he had committed to actually indicating something like that in the article. But, big surprise, it's not in the article and it looks like it's a final report which it's not.

DR. PINKERTON: Regardless, I still think it points out the fact that ozone should be of a primary concern when we think about protecting children's health in the State of California. But if we end up studying PM-10 first, then I think we're going with the flow of the nation, and that's probably not such a bad idea, but don't put ozone on the back burner for too long.

DR. THURSTON: This is George Thurston. My comment that this also is sort of synchronized with the

national effort because the PM criteria document -- the new version is about to come out -- and there have been a lot of generation of new publications in the last couple of years, you know, with pressure to get things published in time to be considered. And now the same process is about to begin with ozone, that the ozone criteria document is now cranking up. So sequentially, I think there will be a lot of interest in publications looking at the question of ozone in the next year or so. So it might be wise to do it in this order so that you have those publications that are going to come out in, I guess, similar to what we have with PM -- maybe to a lesser extent. But there will be a bunch of new publications. And of course E.P.A. will be preparing their document which provides inputs to the process that might be useful and help in the efficiency of getting it done. So there's that federal/State resonance there that sort of, I think, will work to the advantage if you do the PM first. I don't know if that's a critical factor in the decision, but it may be a benefit if that's the way it works out.

DR. SHERWIN: I would like to add a piece of philosophy. One has to do with the hard data. And Dr. Vostal had talked about mortality/morbidity. And I think we have to start paying more attention to what we have termed

"morbility," in other words that same old pyramid, but instead of death at the tip and morbidity a little bit above water, the mass of that iceberg is below water and that's the subclinical disease. It's extraordinary how much subclinical disease you can find. I learned that when I was in the Korean war with young kids of 19 with total occlusion of the left coronary artery, for example. So we know there's vast amounts of subclinical damage in people, and we're not paying much attention to it. If there were some way of getting that kind of data, I'm sure it would be super. And one way, of course, comes to that second point. And that says we need more pathologic data. And with ozone, and one reason I'm convinced that we need to go the PM-10 route first is that we have -- let me read you a simple statement from the last report. It's a pre-print, it hasn't come out yet, but this is a pre-print where we compared Miami and Los Angeles. It was very preliminary limited studies and I apologize for the small amount of data, but the punchline that we gave was, "Cumulative data indicate that expanded pathologic studies are essential for efforts to complete a convergence of epidemiologic and experimental data implicating exceedances of the federal ozone standard as a contributor to human lung injury." Now

that "convergence" comes from David Bates' statement saying, "We now have a nasty convergence of all this evidence and what we need is that missing link, the pathologic." It's all good and well to talk about all these alterations that imply human irreversible damage with longstanding chronicity, but the big missing link is to show people that there is in fact damage. Now I know there's damage, but there isn't any adult lung I look at that doesn't have some degree of emphysema, COPD, or whatever you want to call it, some alteration of airways and air spaces, plus all kinds of other strange kinds of things. So the damage is progressive and every one of us is on that decline, and so the real problem is what I guess somebody else mentioned here before, which was facilitating, promoting, exacerbating the things with human lung injury, which are the things that we have to start really emphasizing in standard considerations.

DR. OSTRO: Yeah, for those people who were concerned about putting one pollutant or the other on the back burner, let me just remind you that according to SB25, we have two years to review and potentially revise the first pollutant, and then one year after that to revise or review a second pollutant. So if ozone and particles are deemed to be the top two priorities, basically we have three years to

review both of those pollutants. So it's not like we have a long time to do all that work. We expecting your help!

DR. KLEINMAN: And don't forget that there are interactions between PM and ozone that need to be factored into the process somehow. So on Tier 1, it seems like PM, ozone, and then NO2 would be next in line.

DR. SHERWIN: May I just add one quick statement since we're now pushing aside nitrogen dioxide? My own personal feeling is nitrogen dioxide is a very important consideration, and interestingly enough, as John Balmes pointed out, John Peters is coming up with more nitrogen dioxide -- I believe -- significance than ozone, and the experimental work that we had done in my lab, and especially with what Dr. [Inaudible] Richards [phonetic] had done with the immunologic approaches, and what we've seen in the lungs, tells me that NO2/NOX just simply can't be ignored. So even though we may go the route of PM-10 and ozone, I think we have to now put that caveat again to say, please, we don't wish to understate the potential importance of nitrogen dioxide, even though we don't seem to be exceeding the standard locally. And with that, I would say, remember, we mentioned that we're going off the .15 24-hour standard, and we restricted it to one-hour. And E.P.A. has an annual

standard which I personally think is totally meaningless. So I think that there are a lot of shortcomings in even the monitoring of importance.

DR. KLEINMAN: Well, taking that caveat into account, that is why it's in the Tier 1 and will certainly be reviewed before the other, the Tier 2 groups, are really considered. In point of fact, all these standards are important. They've all been shown to have health effects to some extent, some more than others. They are going to affect children. So it is important that we get these reviewed, decide whether we have appropriate protective factors for the residents of California. But you can only do one thing at a time or a few things at a time. So prioritization is helpful. It's not the bottom line of it though.

DR. SHERWIN: Michael, could I add a three-second thing that says one of the reasons I go along with this idea of prioritizing is that, in reality, you can't really treat PM-10 alone, or ozone alone, or NO2 alone. We actually will be taking some of those into consideration because they certainly must interact. And your ideas of working with mixtures of particulates in itself emphasizes the fact that we have to be a lot broader in approaching toxicity.

DR. KLEINMAN: All right, on Tier 2, does anyone have any strong feelings about the pollutants in the Tier 2 level?

DR. LIPSETT: Excuse me, this is Michael Lipsett again. Did you poll everybody about NO2 being in the first tier? I mean, does everybody tend to agree with that?

DR. KLEINMAN: We polled and asked if anyone felt that anything should be removed from the first Tier.

DR. LIPSETT: Okay, I missed that. I'm sorry.

DR. KLEINMAN: And nothing from Tier 2 that looked like it should move into Tier 1. But if we look at Tier 2 now, are there any strong feelings about the Tier 2 pollutants which are lead, carbon monoxide, hydrogen sulfide?

DR. SHERWIN: Does that include a question on ranking them? Are you looking for -- DR. KLEINMAN: Well, if you have a feeling for ranking --

DR. SHERWIN: Well, I feel pretty strongly about CO. I think we're not quite tuned into all of the things that CO can do. And considering the tremendous cardiovascular problem we face, and the chronic nonspecific lung disease problem we face, I think that CO is something where I think every household should have a CO monitor

present. And I think if ARB would give me a monitor to put on my car, I would be glad to do my personal recording. But I do think CO is tending to be understated. And don't forget, we have those special circumstances such as higher altitude. There are some people here -- I have colleagues that live at 2-3-4,000 feet in the Los Angeles area. And there are other people, of course, Lake Tahoe -- I think we considered Lake Tahoe to be a special circumstance. So I think there is some uncertainty in CO that warrant special attention.

DR. THURSTON: George just reminded me that -- you started to ask the question if anything should be moved from Tier 2 to Tier 1, but then you said let's go back to Tier 1. I don't know if you formally ask --

DR. KLEINMAN: Oh, I'm sorry. Maybe we didn't formally ask that question then. Thank you for the correction, George. Does anyone feel that we should move something from Tier 2 to Tier 1? For the record, it is not moved. So Russ has suggested carbon monoxide be considered, you know, the Q2's, the higher priority. Does anyone else have any comment on this? I had one thought from what Bart had said earlier. The standards that are least protective. And in terms of the actual position of a standard, the one

that is the most out of line is the lead standard. The particular value for the lead standard is probably well above what we would now consider to be protective. And so although lead per se is not an ambient air problem, at least in most of California, just to have our priorities correct, the lead standard is one that is likely to be revisable. And so perhaps it should be given a relatively high priority, just on the basis of a number that needs to be adjusted. I think that gives you about five years worth of work. And who knows what the science will bring to us in five years? So maybe that's enough of a priority. Are there any other business items that we need to conclude? George?

DR. THURSTON: I just wanted to follow-up on what Russ Sherwin said and to point out that I agree with his motion that probably CO should be the first one of Tier 2 to look at just because there are these new studies, including by Moolgavkar, pointing towards CO as having a role. And of course I think we have the other evidence that was presented and the biological plausibility of CO in terms of cardiovascular problems. So that's my two cents on that. Looking from the epidemiology perspective, I think there is justification for that.

DR. KLEINMAN: On the basis of CO, I would tend to agree with that. I believe that there is a lot more evidence coming out and CO will be something that needs to be reviewed. SO2 -- we haven't really discussed. It does have dramatic effects on asthmatics and I think the sense was that it's certainly an issue of importance, even though our SO2 levels are generally low. Anyone care to comment on the relative importance of SO2 vs. CO within Tier 2?

DR. BALMES: For many years, I've made the comment that the federal standard is not an adequate protective with regard to asthma exacerbations, and the State standard is better. And it's not much of a problem in California, so that's why -- you know, there are still point source issues. Kids could live down wind from a refinery and get SO2 exposures that could cause them to have exacerbations of their asthma. But it seems to me that what I've heard about CO and what I've seen in terms of some of the epi studies that I personally would prefer a review of CO over SO2 at this point. If we had more of a SO2 exposure problem in California, I might feel differently.

DR. THURSTON: And you might recall Jane Koenig's comments yesterday. I think she would have said SO2 first, but just as an aside.

DR. BALMES: She studied a lot of allergic adolescent kids who've had -- she's measured responses of kids to SO2.

DR. THURSTON: Yeah, I think that maybe she was saying it's sort of like the argument for lead, that a short-term SO2 to her is a no-brainer. You ought to just put one in right away or something.

DR. BALMES: I don't disagree.

MS. MARTY: This is Melanie Marty. I just had a comment about the SO2 issue. I was taking to Jane yesterday and it's my understanding that for these asthmatic studies, you don't put severe asthmatics in these chambers, that these are primarily mild, maybe, monitored asthmatics. I think that's something that needs to be considered because there certainly are severe asthmatics out there.

DR. KLEINMAN: Right.

DR. BALMES: John Balmes again. I do think a short term standard for SO2 is a no-brainer, but that issue has been out there for a long time and there hasn't been much movement. If the committee feels that that's something we should push for, I certainly wouldn't have any problem with that.

DR. KLEINMAN: Dane may be able to provide a

little bit more info on this, but when we reviewed the SO2 standard, the one-hour standard was set at a level that took into account the relative number of short-term peaks --

DR. BALMES: In California?

DR. KLEINMAN: In California. So it may have built into it sufficient safety for those short-term exposures, or at least a consideration. And at the time, the major reason for taking the one-hour vs. 15 minutes was basically data. You know, management problems rather than the ability to measure it.

MR. WESTERDAHL: Dane Westerdahl. The answer is correct. The health information that U.C.S.F. generated indicated that .25 was definitely an effects level over a one-hour average, that some of the subjects responded. And this was an open chamber. There was discussion yesterday about face masks. This was an open chamber. But there were also individuals who had measurable decrements at .1, so there was no margin of safety in the standard. There were questions as to why the maximal response was in three to five minutes, as I recall, in these studies. There was a question why didn't we set a shorter term standard. I think at that time, people involved in monitoring were very reluctant to deal with data in three to five-minute

increments. Even though it could be done, they were very reluctant to do it. That's not a reluctance any longer. It could be done more easily now. Everything is on line. And again, John knows this information very well. There is no health protection at the .25 one-hour average. That's the effects level and people are effected below that.

DR. PINKERTON: Mike?

DR. KLEINMAN: Yes, Kent?

DR. PINKERTON: From the perspective of those of us who study animals to understand air pollution, certainly SO2 would seem more logical for us to be wanting to look at, and especially relating it to asthmatic-like conditions, but I think the logic here really does dictate that probably the CO is the major pollutant on the second tier that would be the one that should receive the priority.

DR. KLEINMAN: I'd like to invite any further comments from the floor if anyone else had comments on the relative structuring of these Tiers. Suggestions? Bart, do you have any closing remarks you'd like to make?

DR. OSTRO: Yes, some very simple ones. First of all, I wanted to thank the scientists who have come here today and yesterday to help us review these pollutants. And George, the one remaining long distance hold-out, a special

thanks for hanging in there and providing some input for us. Thanks to you, Michael, for helping narrate and moderate. Thanks to the Court Reporter and sound person, and to Rachel Broadwin again for helping to organize all of this. And we appreciate all your help.

DR. KLEINMAN: Thank you. I'd like to thank especially Rachel, Mike and Bart for coordinating this effort. I think putting this effort together has been a very good experience. It's provided a very useful document and I think the State is moving in the right direction, thinking about protecting children's health, and we certainly want to be supportive of that. I would like to invite the members of the committee if they've got specific comments that have not been given -- editorial things related to the specific projects or the specific articles -- that we get those in to Rachel. Is that okay? And she will distribute them to the authors so that they can be incorporated in the final version of the papers. And if transparencies were used during the presentations here, it would be extremely useful for us to have copies of those, and those can also be given to Rachel. And I believe with that, I'd just like to again extend my thanks to the Committee, the consultants, the authors, and to everyone

else here because it's really been a very good interactive experience. I believe a lot of information has been exchanged. So with that, I'd like to close this session and adjourn. Thank you very much.

(Adjourned.)